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Archives of Neurology and Psychiatry

VOLUME 21 FEBRUARY, 1929 NUMBER 2

AMAUROTIC FAMILY IDIOCY AND GENERAL LIPOID DEGENERATION *

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NEW YORK

An apology might be needed for bringing this subject once more before this Association. I should hesitate to speak of my pet son if it were not that after a vigorous youth of forty years he surprised me by forming new and interesting contacts. These contacts were revealed through the work of Ludwig Pick,[1] ably seconded by Max Bielschowsky.[2] In the gradual development of these new alliances the work of Mandelbaum,[3] of Bloom [4] of Chicago, of Niemann [5] and of a number of others [6] has been helpful.

The clinical features of the infantile form of amaurotic family idiocy are fortunately so well established that nothing need be added; the Tay-Sachs type has been universally accepted. Of all the cardinal symptoms, the most puzzling one, in my opinion, has been the unusual and rapid emaciation of the child. At the beginning, the majority of these children are plump and well developed; in the course of a year, many of them are reduced to skin and bones. This one fact should be kept in mind.

* Submitted for publication, June 18, 1928.

* Read at the Fifty-Fourth Annual Meeting of the American Neurological Association, Washington, D. C., May 1, 1928.

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2. Bielschowsky, Max: Zur Histopathologie und Pathogenese der amaurotischen Idiotie mit besonderer Berücksichtigung der zerebellaren Veränderungen, J. f. Psychol. u. Neurol. **26**:123, 1921; Amaurotische Idiotie und lipoidzellige Splenohepatomegalie, J. f. Psychol. u. Neurol. **36**:103, 1928.

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4. Bloom, William: Splenomegaly (Type Gaucher) and Lipoid-Histiocytosis (Type Niemann), Am. J. Path. **1**:595, 1925.

5. Niemann, A.: Ein unbekanntes Krankheitsbild, Jahrb. f. Kinderh. **79**:1, 1914.

6. Knox, J. H. M.; Wahl, H. R., and Schweisser, H. C.: Gaucher's Disease; a Report of Two Cases in Infants, Bull. Johns Hopkins Hosp. **27**:1, 1916. Oberling, C., and Woringer, P.: La maladie de Gaucher chez le nourrisson, Rev. franç. de pEdiat. **3**:475 (Aug.) 1927.

The structural changes developed in the course of the disease are equally definite. To be sure, forty years ago I thought the cellular changes were restricted to the cerebral cortex. By degrees, and through the cooperation of many able workers, the same cellular changes were found throughout the central nervous system and in the spinal ganglia. Years ago, I was able to claim that scarcely a normal ganglion cell was to be found. The huge increase in the size of the cell, the vacuolization, the disappearance of the nucleus or its complete dislodgment, the distortion of the entire cell mass and the swelling of the dendrons were characteristic of the disease. A few years ago, Bielschowsky, and possibly one or two writers before him, began speaking of the deposit of a lipoid substance within the cells; Bielschowsky insisted that the pathogenesis of the disease must be linked with the source of this substance. Acceptance of this view implied opposition to the conclusions of Schaffer, who supposed that the lecithinoid granules found with startling uniformity in all the nerve cells of the central nervous system in this disease were to be regarded as products of degeneration. According to Schaffer, the disease process is confined chiefly to the ectodermal elements. He claimed that congenital weakness of the ectodermal layer is the fundamental characteristic of all heredodegenerations.

In the meantime, clinical and pathologic studies have revealed a surprising relationship with another group of diseases—with Gaucher's disease and with a familial and fatal disease of infancy showing great predilection for the Hebrew race and bearing some, if not complete, resemblance to Gaucher's disease, spoken of as a lipoid cellular splenohepatomegaly, or, as Bloom called it, lipoid histiocytosis (type Niemann), an infantile type now known as the "Niemann-Pick type" in contradistinction to the Gaucher type. Both types would appear to be variants of a general lipoid cellular degeneration with enlargement of the spleen and liver. The Gaucher type may occur at any age. The Niemann-Pick type is an infantile type terminating fatally before the end of the second year. In the Gaucher type, the lipoid invasion affects the reticular cells and the connective tissue cells, the so-called histiocytes. In the Niemann-Pick type, the same invasion occurs not only in the entire reticulo-endothelial apparatus, but also in the elements of all other body tissues—in the muscles, in the glia, in the ganglion cells and in all epithelial cells, even in the cells of cartilage. If the similarity of these two types is to be acknowledged, I might be tempted to call the Gaucher type the juvenile and the Niemann-Pick type the infantile form of this splenohepatomegaly, thus emphasizing the resemblance of these forms to the two types of amaurotic family idiocy; until, however, all the facts shall have been gathered beyond the shadow of a doubt, I put this general resemblance forward with considerable reserve. The underlying disease process in all these forms is

evidently a profound and primary disturbance of metabolism. That may be accepted at the present time. It is Pick's contention that in the Tay-Sachs type the same disturbance in lipoid metabolism is the predominant factor. When this metabolic disturbance affects the entire body, the Niemann-Pick type, a universal disturbance of lipoid metabolism is developed; the Tay-Sachs type is a disturbance of the same kind restricted to the nervous system.

Before the evidence in support of these views is weighed, it may be well to give a brief summary of the two main types with which I am concerned. Gaucher's disease is a relatively rare condition, characterized by marked chronicity, by a distinct anemia, a slight tendency toward bleeding, a brown-yellow pigmentation of the skin, enlargement of the spleen and cirrhosis of the liver without ascites. Histologically, it is characterized by peculiar large pale cells which also occur in other parts of the hematopoietic system and are now generally supposed to be derived from cells of the reticulo-endothelial system. Incidentally, it is interesting to recall that, in 1882, Gaucher described the disease and thought it to be a primary epithelioma of the spleen. Many years later (1914), Niemann,[5] in discussing an "unknown clinical picture," found cases which bore a general resemblance to Gaucher's disease, but which presented also certain marked differences. This disease occurred in very young children, the first symptoms appearing as a rule in the first three or five months of life. It was distinctly a familial disease, and girls seemed to be affected more than boys. It was also established that the disease occurred particularly in the Jews, and was characterized by a peculiar brown color of the skin and enlargement of the spleen and liver, with an almost normal blood picture. The definite diagnosis rested on the storage of lipoid material in certain cells, and material removed by puncture of the spleen was supposed to be essential to a correct diagnosis. Splenectomy was performed in several cases. In one case especially, of Bloom, an improvement was brought about, but death ensued six months later. Ludwig Pick took up the study of this group and during the last four years has described the peculiar histologic changes so accurately that subsequent authors now speak of this type as the Niemann-Pick type. Unfortunately, internists and neurologists were miles apart in their earlier studies. Bloom [4] in his paper, published in 1925, said of one of his cases that there was a distinct pupillary immobility to light, and in another case that the eyegrounds showed the changes known to exist in amaurotic family idiocy. General clinicians paid little attention in their autopsies to the nervous system, and I think that neurologists neglected the minute histologic examination of the abdominal organs. I am certain, however, since others like myself had the opportunity to examine the abdominal organs again and again, that an enlarged spleen and an enlarged liver could not have escaped

observation. It is entirely due to Pick's careful examination and to his keen observation that the similarity between these two conditions has been brought forth so prominently. It is extremely interesting to me to read in Pick's recent publications, speaking of a child of the Niemann-Pick type, that the brain of the child is surprisingly hard. It is so firm that it "stands on the post-mortem table," its weight is 700 Gm., "the convolutions small, and the fissures deep." I am reminded of the remark which I made [7] regarding the first brain of a person with amaurotic family idiocy that I examined, that it was so hard that the knife "grated in cutting."

Without plunging too deeply into all the mysteries of splenohepatomegaly, it is of interest to know that in his last publications Pick recorded several cases of the Niemann-Pick type in which he made a complete examination of all the organs, including the central nervous system; he also recorded that one of these cases was easily recognized as a form of the Niemann-Pick type, in which all of the cardinal symptoms of the Tay-Sachs type were present. Without wishing to add to the complexity of the subject, let me record that Pick regards the Niemann-Pick type as a disturbance of the phosphatid and especially of the lecithin metabolism, whereas in Gaucher's disease the disturbance of lipoid metabolism is caused by kerasin. One is plunged headlong into the mysterious and complex questions of cell chemistry. Before deciding whether or not one is to accept the relationships of amaurotic family idiocy to the Niemann-Pick type, it will, of course, have to be shown that the symptoms of amaurotic idiocy occur in a relatively large number of cases of the Niemann-Pick type, and it will be still more important when one has the occasion to examine all the organs of a child dying of amaurotic family idiocy to prove that in those cases the histologic cellular changes in the abdominal organs are similar, as Pick believes, to the cellular changes that are now so well known as occurring in every part of the central nervous system. In their latest presentation of the subject, Pick and Bielschowsky hold that, like Gaucher's disease, the Niemann-Pick type is a primary metabolic disturbance in the course of which the overloading of the blood and of the connective tissues with lipoid material mobilizes the entire macrophage apparatus of the body. After complete saturation and exhaustion of these tissues the lipoid material overflows into and invades all other body tissues, thus abolishing the function of all the vital organs and causing fatal exhaustion.

The disease for which I have stood sponsor for so many years seems to me to have acquired additional interest, and I have brought up this matter in the hope that any one who has occasion to see typical cases

7. Sachs, B.: On Arrested Central Development, J. Nerv. & Ment. Dis. **14**: 546, 1887.

of amaurotic idiocy will pay especial attention to the careful microscopic examination of every organ and tissue of the body, even including the bone marrow. I need not give assurance that I shall watch this question rather closely so long as possible; but granted that there is this resemblance between these various types and that there is this startling disturbance of lipoid metabolism, and that the amaurotic idiocy may have to be taken out of the category of hereditary and degenerative diseases and classed among the primary metabolic disturbances; granted all this, the mystery still remains; what is the underlying factor of a constitutional familial hereditary and peculiarly restricted disease that causes this disturbance? May it after all in some mysterious way be linked to one or more of the endocrine glands, and then what? Possibly one may obtain a clue as to useful therapeutic measures. That the endocrine glands may possibly have something to do with the disease I have long suspected; the only cases in which the progress of the disease seemed to have been checked for a time were cases of children that were for a time fed on various glandular extracts.

In conclusion, let me say that I am particularly pleased to think that the study of amaurotic family idiocy has once more led to a close relationship between neurology and general medicine.

ABSTRACT OF DISCUSSION

DR. A. FERRARO, New York: It is encouraging to hear such an authority as Dr. Sachs speak in connection with neuropathologic changes in terms of physiologic chemistry. Personally, I believe that besides the morphologic histology one must take into account the histochemical aspect of neuropathology, and I think that other investigators believe this also. Investigations along these lines will open, I believe, a large field to new substantial results.

In regard to Tay-Sachs' disease, Marinesco has conducted biochemical studies of the problem, reaching the conclusion that the disease is the expression of a disturbed process of oxidation. He did find that the nerve cell showed a marked reduction of the so-called "oxydases," oxidizing ferments, which appear to be in proportion to the increase of the lipoproteins. Among these, lecithins, cephalins and cerebrosids play an essential rôle, as following a process of hydrolysis the number of their molecules increases largely. As these molecules have a tendency to absorb water an endosmotic process then originates, thus allowing water to penetrate from the outside into the cell body. The increase in carbon dioxide content, a result also of faulty oxidation, increases the endosmotic process. That the disturbance in oxidation does really take place is also proved by the fact that the content in glycogen of the nerve cells and neuroglia cells is definitely increased, thus pointing again to a defective oxidation.

All these facts become more interesting in the light of the new data which Dr. Sachs has given connecting Tay-Sachs' disease with general lipoid degeneration. Biochemical processes seem to be at the base of such an important disease. But while in the Tay-Sachs' form the morphologic changes are found alongside the histochemical changes, it is possible that other diseases, especially mental ones, may disclose histochemical disturbances which are not accompanied by morphologic changes.

Dr. W. G. Spiller, Philadelphia: I have been intensely interested in what Dr. Sachs has said. I think that he has opened up a great field from the observations which he has made. It has interested me in getting to the fact that the liver has a great influence in this disease. Dr. Sachs' statements show clearly how one must study the general system of the body in order to explain this type of disease, and one will thus get further information.

Dr. Israel Strauss, New York: Dr. Sachs forgets that at one time, in writing an article following Dr. Schaffer's contribution, he made the statement that this disease, the Tay-Sachs' disease, is due to some fundamental biologic change in the patient and possibly that it had some relation to metabolism.

One point I would like to make is this: In staining these sections with scarlet red—I am speaking of amaurotic idiocy—and likewise in staining the livers and spleens in Gaucher's disease with scarlet red, one gets no reaction. Hence the change in these cells does not result in producing a fatlike body which can be stained with scarlet red. There is no question but that it is a lipoid-like body. I can say that because the late Dr. Mandelbaum at the College Hospital did a great deal of work on Gaucher's disease. He stained many of those sections in order to demonstrate the presence of fat in that disease, but was unable to do so.

Furthermore, I have had experience in staining and examining the spleen in many cases of amaurotic idiocy and never found anything approaching the picture of Gaucher's disease. Neither Dr. Sachs nor I found any cases in which a spleen or liver was pathologically enlarged. That does not say that that symptom does not exist in this disease.

There are, moreover, two more points of differential diagnosis. In Niemann's disease there is an extremely severe anemia. Gaucher's disease may be associated with a form of anemia. I have never seen an anemia other than a mild secondary anemia in amaurotic family idiocy. In other words, in certain of these diseases the bone marrow must be affected more than it is in others. Unquestionably, one is dealing with a process which is similar in the three conditions. It is unquestionably a process which has to do fundamentally somewhere with lipoid metabolism. In the fetus the suprarenal is a tremendously large organ and has a great deal to do with lipoid metabolism; as the brain develops the suprarenal becomes smaller. That has been clearly shown by Aschoff. It might be worth while studying these organs in connection with these diseases. I am sorry that Dr. Sachs turns to the endocrine glands for an explanation; those organs have had much to bear in the last few years in medicine. Every unknown condition that occurs in neurology or in medicine today, it seems to me, is passed over with the thought that possibly the endocrine glands are responsible.

Dr. S. E. Jelliffe, New York: I am tempted to add another speculation to the numerous ones that have preceded and to ask attention to reversal of Dr. Spiller's statement that it is "rather interesting to see that we as neurologists are commencing to understand the relationship between the 'liver and the brain,' as found in lenticular degenerations." I should like to turn this thought around and say that sometime perhaps we may get interested in the relationship between the "brain and the liver," namely, to obtain a wider grasp of what the coordinating mechanism which we call the nervous system is doing to the innumerable series of stimuli that are coming from the external world, and which are collected in various organs of the body.

If I may I would bring to the attention of some of you a few remarks that I made before the Research Society when we were discussing the heredodegenerations. At that time I tried to emphasize the fact that the Tay-Sachs' family amaurotic idiocy showed perhaps to a preponderant degree the falling out of a whole system connected with light reception. In this disorder it is not alone the optical receptors

that are unable to handle the light from the external world, but other light receptors in the body are also cut off. The entire chromatophore system, that is, the pigment cells beneath the skin, are receiving organs for light stimuli. Some of us have been very much interested in studying not only the embryology of these chromatophores, but also their histochemistry, especially as to such chemical affiliations between the chromatophores of the skin and the suprarenal systems. It is well known that the suprarenal system and the sympathetic system are intimately related, but until Bloch did his work on skin pigments it was not appreciated that skin pigment, suprarenals and sympathetics were a chain from simple to complex of closely related dynamic functions. Dr. Strauss' remarks about the suprarenals in this syndrome, therefore, come into the picture, and it seems to me that although the suprarenals may be involved in the causal relationship, I agree with Dr. Strauss that we should not put any more burdens on the endocrine glands as causative factors than they can bear; but by reason of the fact that not only the skin but also the eye receptors do handle the light energy streaming into the human body, there results a widespread degeneration of all the tissues of the body and therefore a corresponding loss of the upper cerebral machinery that would serve to coordinate this material. Hence, when Dr. Sachs would call attention to the somatic side of a central nervous defect, he is but completing what is to be expected, since the brain, in the sense we are speaking of, is but a central committee of its peripheral somatic constituents.

DR. BERNARD SACHS: While I have had this whole subject in mind for more than forty years, I have not come to any positive conclusions on many points. I agree with Dr. Jelliffe, who made the remark this morning, "Why make conclusions?" I think it is dangerous to come to definite conclusions on anything. I have been entirely receptive to any suggestion that has been made during all these years, but I have had to dismiss some. The suggestion was made that the disease was due to mother's milk. This was rejected at once. Several of the children were not breast-fed. Particularly at the time when Dr. Strauss and I published that paper on "Cell Changes in Amaurotic Family Idiocy," we were under the influence of the doctrines formulated by Schaffer; but when everything was explained on a heredodegenerative basis, I had my doubts about it. I thought that there were certain mysterious changes going on in those cells that none of us as yet understood.

This suggestion of the Neumann-Pick type came to me with a great deal of force; particularly, after I had seen the striking specimens of Pick in his own laboratory and the specimens of Bielschowsky, the resemblance was borne in on me with great force; it would be hard for me to disregard entirely a possible relationship between these two conditions. On the other hand, I am not willing to abandon my child altogether and say that it belongs to other parents, but I should be proud if it has dignified relatives.

I do not want to be misunderstood; what I say is this: I still believe in the fact, which Dr. Strauss also mentioned, that if there had been great changes in the abdominal organs in our cases, they could not have escaped us. The organs were normal, but the staining methods in those days were not nearly as perfect as they are today, and even Mandelbaum, who was an extremely careful histologist, could not prepare the beautiful specimens that can be prepared nowadays, so that the evidence was not as good then as it is today.

I do not believe that amaurotic family idiocy is always associated with the Neumann-Pick type of disease. I believe that it has an independent existence. But the thought that is in my mind now is that if this disordered lipoid metabolism affects the entire body, the Neumann-Pick type of disease may occur. If it is restricted to the nervous system, as I believe it more often is, then an amaurotic family idiocy (the Tay-Sachs' type) will be developed.

PLURIGLANDULAR SYNDROME

INVOLVING CALCIUM DEFICIENCY AND CORRELATED WITH BEHAVIOR DISTURBANCES*

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Within the past ten years many cases have come under my observation in which the chief complaints were those of incorrigibility, nonamenability to discipline, and assaultiveness; the patients were easily aroused to a high pitch of anger at the slightest provocation—a word, an insinuation or even a glance being sufficient to arouse intense antagonistic reaction. These patients became problem cases at home, at school or in whatever environment they found themselves, because of their nonadaptability and uncompromising attitude. Occasionally their behavior became so exaggerated that apparently hypomanic states developed therefrom, and several of these patients had to be confined in institutions until the symptoms were ameliorated. At home, a harsh word from any member of the family, at the table for instance, would result in a plate or knife or some other utensil being thrown at the aggressor. In school, a blow, a shout or a curse would be hurled at a fellow student, or even at the teacher. Because these patients seemed to the observer to have many points in common, such as stature, bodily features and biochemical conditions, it seemed important to determine whether they formed an actual group which could be differentiated by certain stigmas, in both the physical and the biochemical domains. I have collected the reports of a representative group of such cases and have arranged and classified the observations to bring out some of the common correlated features.

MYOTATIC IRRITABILITY AND MYOIDEMA

Practically all the cases, in both children and adults, showed the physical signs of myotatic irritability and myoidema, some to a greater degree than others. In some, the myotatic irritability would be increased to such a point that a Chvostek reaction of moderate degree was obtained. From experiments made by a number of investigators, notably McCallum and Voegtlein,[1] it has been shown that muscle irritability and excitability is due largely, if not entirely, to a diminution in the utilization of calcium. The unanimity with which myotatic irritability was found in

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* Read at the Fifty-Fourth Annual Meeting of the American Neurological Association, Washington, D. C., May 1, 1928.

1. McCallum and Voegtlein: The Relation of Tetany to the Parathyroid Gland and to Calcium Metabolism, J. Exper. Med. **40**:118, 1909.

this entire group of cases is striking. The converse, however, that all patients with myotatic irritability and myoidema have the behavioristic qualities shown by patients in this group is not true to the same extent, but the attributes are nevertheless sufficiently prevalent to awaken suspicions of conduct disorders whenever these physical signs are evoked. The best site for eliciting both myotatic irritability and myoidema is at the shoulder over the deltoid and pectoral muscles.

TABLE 1.—*Observations on Patients Under Sixteen Years of Age*

Blood Calcium		**Blood Sugar**	
5 to 6 mg. per 100 cc.	6	120 to 140	5
6 to 7 mg. per 100 cc.	9	110 to 120	7
7 to 8 mg. per 100 cc.	4	100 to 110	1
8 to 10 mg. per 100 cc.	4	Below 100	2
Blood Pressure		**Pineal Shadow**	
Above 120	5	Present	14
110 to 120	5		
100 to 110	4	Absent	5
Below 100	3		
Growth Defects			
4 inches (10.16 cm.) or more below average height for age			9
2 to 4 inches (5.08 to 10.16 cm.) below average height for age			4
Normal			6

TABLE 2.—*Observations on Four Patients with an Apparently Normal Blood Calcium*

Name	Age	Sex	Blood Calcium	Myotatic Irritability Myoidema	X-Ray Examination	Other Glandular States	Behavior	Other Symptoms
J. L.	5	M	10.0	Marked	Persistent thymus needing x-ray at 8 months; sella quite small	.....	No self-control; violent temper; tantrums	Fatigue
J. Y.	9	M	10.6	Marked	Persistent thymus; x-ray treatment of thymus at 8 months	.....	Uncontrollable and violent; lack of self-control; domineering	Fatigue
G. B.	8	M	10.5	Myoidema	Sella slightly smaller than normal	.....	High temper; deficient; irritable	Fatigue
J. C.	14	M	9.9	Marked	Pineal calcified; thymus present	Large genitals	Assaultive; bad; incorrigible; undisciplined	Fatigue

UTILIZATION OF CALCIUM

Because of the correlation between muscle irritability and non-utilization of calcium, I next undertook the examination of the calcium content of the blood. In the laboratory examination, the calcium content of the whole blood is determined—not merely that of the serum. The normal values are from 6.5 to 9.5 mg. per hundred cubic centimeters of whole blood. From the tables it will be seen that nineteen of the twenty-three cases showed deficient blood calcium, varying from 5 to 8 mg. per hundred cubic centimeters. The four cases that showed

an apparently normal blood calcium are of interest for the reason that treatment, as will be hereafter indicated, was just as efficient in them as in the other nineteen cases that showed deficient blood calcium. This led me to suppose that it was not so much the presence of calcium in the blood that determines the disturbances as it was the utilization of calcium which under treatment seemed generally to be increased. It is curious to note that in many of the cases in which a low calcium content was observed in the blood, there was an increased deposit of calcium in various portions of the body producing thick skull tables, and particularly that there were calcium deposits in the pineal gland.

Pineal Calcification.—It is interesting to note that of nineteen cases in which the skull was examined with the x-ray, fourteen showed a

TABLE 3.—*Observations on Adults*

Name	Age	Sex	Blood Calcium	Myotatic Irritability, Myoidema	X-Ray Examination	Other Glandular States	Behavior	Other Symptoms
A. P. D.	20	M	5.4	Marked	Enlarged pituitary	Thyroid full	Easily aroused and then so blocked he cannot talk; excitable	Fatigue; trismus; muscle cramps
E. C.	26	F	6.0	Marked	Pineal shadow; small pituitary	.....	Cannot concentrate; mind tense and immobile	Fatigue; scant menses; tense
C. B. D.	46	F	6.8	Marked	Exceedingly thick skull tables	.....	Excitable; uncontrollable	Fatigue; urticaria; tense; no relaxation

pineal shadow in spite of the fact that the patients in all were 16 years of age or less—a comparatively rare observation. Whether the pineal calcification is merely a part of the calcium metabolic disturbance in the patient or whether it represents a pineal involutional process is difficult to say. If it represents a pineal involutional process, one would expect to find some structural or metabolic effect. As a matter of fact, in five of my cases in which a pineal shadow was shown, there were such symptoms as enlarged clitoris and breasts (one case), pubertas praecox (one case) and enlarged genitalia in boys (three cases). In several others, psychosexual precocity was pronounced. Whether or not the pineal effect on muscular activity,[2] as has been stated, is a fact, it is interesting to note that a large percentage of my cases showed intense muscular fatigability (table 1).

2. Timme, W.: Progressive Muscular Dystrophy, Arch. Int. Med. **19**:79 (Jan.) 1917.

GROWTH

The next interesting observation in these cases pertains to growth in length. Of nineteen cases, six of the children were of normal height, four were between 2 and 4 inches (5.08 and 10.16 cm.) below average

TABLE 4.—*Observations on Fourteen Children Under Sixteen Years of Age*

Name	Age	Sex	Blood Calcium	Myotatic Irritability, Myoidema	X-Ray Examination	Other Glandular States	Behavior	Other Symptoms
G. M. W.	15	M	6.1	Excessive	Pineal calcified; small sella; thick skull tables	Enlarged genitalia	Manic outbursts; uncontrollable	Great fatigue
J. G.	11	M	6.2	Excessive	Pineal calcified; small sella	.....	Assaultive; incorrigible; threw knife at father	Great fatigue; muscular cramps
R. Go.	11	F	7.1	Very marked	Pineal calcified	Enlarged clitoris and breasts	Incorrigible; assaultive; curses	Fatigue
R. Gn.	11	F	6.8	Very marked	Pineal calcified; very small enclosed sella	.....	Quarrelsome; assaultive; unmanageable	Fatigue
V. S.	14	M	7.5	Marked	Pineal calcified; thick skull tables	Enlarged genitalia	Tenseness; easily angered; stammers	Fatigue; still has deciduous teeth
D. H. E.	16	M	7.8	Very marked	Small, enclosed sella	.....	Assaultive; forges checks; police case	Fatigue
N. S. L.	16	M	7.1	Excessive	Pineal calcified	Thyroid enlarged	Incorrigible; easily angered; curses	Fatigue
M. F.	15	M	7.2	Very marked	Pineal calcified; small enclosed sella; thymus enlarged	.....	Irritable; incorrigible; stammers	Fatigue
J. W.	9	M	6.2	Excessive	Small sella; convolutional digitations	.....	Impatient; easily angered; quarrelsome	Fatigue; headache
J. M.	15	M	7.2	Excessive	Craniostenosis; oxycephalic; thick skull tables	Thyroid full	Easily excited and keyed-up; extreme tenseness	Fatigue; tenseness of muscles of neck
J. G.	12	F	6.8	Excessive	Pineal calcified	Menses at 11; pubertas praecox	Incorrigible; volent temper; curses	Thyroid full
A. B.	14	M	6.9	Very marked	Pineal calcified; thymus enlarged	.....	Incorrigible; undisciplined; assaultive	Retarded I. Q. 80%, fatigue
M. C.	14	M	5.9	Excessive	Pineal calcified; thick skull tables	Enlarged genitalia	Violent temper; irresponsible	Poor muscular coordination
V. A.	7	F	5.9	Marked	Digitations more than normally visible	.....	Intelligence quotient 58%; cannot talk; excitable	Fatigue

height for age, and nine were 4 inches (10.16 cm.) or more below the average height for age; these figures show a tendency toward dwarfism. When one realizes that the utilization of calcium is deficient, one can readily understand how part of nonutilization might readily have affected the growth of the long bones (table 1). Treatment, as will appear, tended to increase rapidly the growth of some of the patients.

OBSERVATIONS ON THE BLOOD

Blood Sugar.—Running in inverse proportion to the calcium is the sugar content of the blood. Only two of my patients had a sugar content below 100 mg. per cubic centimeter; the blood sugar of twelve being between 110 and 140, and this occurred in subjects under 16 years of age. A low calcium content in combination with a high content of sugar in the blood has been noted by some observers in some types of diabetes, although in none of my patients was glycosuria present[3] (table 1).

Blood Pressure.—Although the patients whose cases are here used as illustrations were 16 years of age or under, fourteen of seventeen had a blood pressure above 100, ten above 110 and five about 120; one girl, 11 years of age, had a systolic pressure of 140. Whether the high content of sugar in the blood and the high blood pressures are secondary to sympathetic disturbance, involving perhaps also the suprarenal or the pituitary glands is to be considered. Indeed, with the rather high sugar mobilization, both suprarenal and pituitary glands might well be considered in connection with the comparatively high tension (table 1).

MENTAL SYMPTOMS

Behavior.—All of the cases were classified on the one basis of behavioristic qualities. As already stated, these varied from the simply incorrigible and quarrelsome ones to those performing assaultiveness and exhibiting the most violent temper, reaching the point of hypomanic disturbance. Whether these behavioristic qualities are due to defect in the utilization of calcium or to some other factors that have been discussed, is a moot point. It seems to me, however, not only because the low utilization of calcium is the most constant factor, but also because of the effect of nonutilization of calcium on the muscular system, that the behavioristic anomalies may belong to the same category, depending on the nonutilization of calcium by the nervous system. It has been shown by a number of previous investigators[4] that diminution in the supply of calcium to the blood results in increased reaction of nerve tissue to an induction current. It is possible that the same factors that bring about myotatic irritability in the muscle, also bring about untoward reactions in the nervous system. That is to say, reaction follows stimulus so rapidly that the overt act is committed before reason and judgment can come into play for purposes of inhibition.

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3. Kahn, M., and Kahn, M. H.: Lime Deficiency of Diabetes, Arch. Int. Med. **18**:212 (Aug.) 1916. Wishnofsky, Max: Studies in Calcium and Carbohydrate Metabolism, J. Lab. & Clin. Med. **13**:133 (Nov.) 1927.

4. Chiari, R., and Froehlich, A.: Zur Frage der Nervenerregbarkeit u. s. w., Arch. f. exper. Path. u. Pharmakol. 110, 1911.

This speed of nerve reaction is perhaps also the basis for the wit and precocity shown by these persons—a property which they all possess.

Intelligence.—For the most part, not only are these patients remarkably witty and precocious in replies and reactions, but they are, in the main, intelligent as well. Theirs is not the incorrigibility and bad-temperedness of the moron and the defective, for on psychometric test in all of my cases only one subject showed an intelligence below normal (intelligence quotient 58 per cent, case V. A.). Indeed, in school, these children were among the brightest and highest in scholastic standing.

TREATMENT

Because of the manifest calcium disturbance, all my patients were treated at first basically and primarily with calcium in varying doses with little effect, although at times reports of improvement were made, which with difficulty could be substantiated at either clinic or office. I then added in the earlier cases, for the generally accepted theory of its specific action in calcium metabolism, a parathyroid preparation in the usual commercial tablet form. Here again, some effect was really observed: a reduction in the intensity of the muscular reactions as well as in the conduct abnormalities was noted. Finally, a few years ago, I obtained for experimental purposes Collip's parathyroid extract which was said to represent the active principle of the parathyroid gland.[5] This preparation was given hypodermically in doses varying from 5 to 7 minims. The effect was noteworthy: the tenseness, the myotatic irritability, the conduct disorders were rapidly ameliorated; growth increased in speed; the calcium content of the blood was increased to normal ratios—and these effects were noted as well in cases in which the patients had apparently a normal calcium content of the blood as in those with low calcium values. (From this the conclusion was drawn that it was not necessarily the calcium content of the blood that mattered, but the utilization thereof that was of importance—the parathyroid gland producing this utilization.) I now have outlined a well formulated treatment consisting of calcium lactate by mouth, parathyroid extract-Collip hypodermically and direct or artificial sunlight regularly administered. The results warranted all these measures, for all the patients improved, though in different degrees. Adults were benefited also, with some exceptions the reasons for which I have not been able to determine. The basis of the treatment, I think, is the administration of parathyroid extract-Collip for on it turned the success of therapy.

A word should be added on the danger attendant on the possible hypercalcemia produced by this treatment. Hypercalcemia causes

5. Collip, J. B.: The Calcium Mobilizing Hormone of the Parathyroid Glands, J. A. M. A. **88**:565 (Feb. 19) 1927.

nephritic irritation as evidenced by albuminuria with casts and must be guarded against by frequent urinalysis and examination of the calcium content of the blood. One safe method, which I pursue, is to give the parathyroid extract-Collip for two weeks with an interval of freedom for one week.

GENERAL SUMMARY

A number of patients presented close resemblances to one another in several important particulars: gross behavioristic abnormalities, with deficient utilization of calcium, parathyroid deficiency and pineal involvement, and with secondary disturbances in growth, blood pressure and gonadal development. This syndrome is easily recognizable, is frequently encountered and lends itself to therapeutic attack.

TUMORS OF THE SPINAL CORD WHICH PROJECT INTO THE POSTERIOR CRANIAL FOSSA

REPORT OF A CASE IN WHICH A GROWTH WAS REMOVED FROM THE VENTRAL AND LATERAL ASPECTS OF THE MEDULLA OBLONGATA AND UPPER CERVICAL CORD *

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Growths that lie both in the uppermost part of the vertebral canal and in the posterior cranial fossa are comparatively rare. Of 185 cases of tumor of the spinal cord verified by operation, in the experience of one of us, seven, or 3.7 per cent, lay both above and below the foramen magnum. New growths in this location are due either to a downward extension of a tumor which began in the posterior fossa of the skull or to one that originated within the vertebral canal and that has grown into the cranial chamber through the foramen magnum.

We have encountered six instances of extramedullary tumor in this location, one of which was so unusual that it is here reported in detail.

REPORT OF CASE

Clinical History.—Mrs. R. H., aged 36, was admitted to the neurologic service of Mount Sinai Hospital, under the care of one of us, on Oct. 19, 1927. She had been first seen by one of us on April 16, 1926. At that time, she gave a history of having suffered from headaches for a number of years but said that they had become particularly severe in the past four years. She described the pain as located in the back of her head and on the left side. The pain had been almost constant for a considerable time, and she could not obtain relief unless she took a brand of amidopyrene U. S. P. Because of this headache she was operated on for some condition of the sinuses five years previously, and following this a tonsillectomy was performed, but relief did not result. An oculist had even prescribed glasses for the headache.

The examination made at that time did not reveal physical signs of any involvement of the nervous system. The x-ray of the cervical vertebrae showed a slight osteo-arthritis of the second and third vertebrae. Pressure on the left suboccipital nerve caused excruciating pain. The diagnosis made then was that she might possibly have spondylitis causing an irritation of the left suboccipital nerve. It was suggested that an injection of alcohol be made into the nerve for relief The patient consulted a physician, who injected saline solution into the region of the nerve without any relief.

She was next seen on Sept. 12, 1927. In the interval between the two visits, the attacks of pain commenced to radiate down the left upper extremity, and dur-

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* From the Neurological and Surgical Services of Mount Sinai Hospital.

ing the last month, the patient noticed a slight clumsiness and weakness of the left upper extremity, which had been increasing. She also commenced to suffer from paresthesias in the fingers of the left hand. Disturbance of the function of the bladder or bowels had not occurred.

At the second examination, she showed a distinct weakness of the left arm and left leg, and a Hoffman sign in the left hand; the knee jerk of the left leg was much more active than the right; left ankle clonus, with a left Babinski sign and diminished sensation on the left side of the neck in the region of the second and third cervical dermatomes was present. A diagnosis of a high cervical neoplasm was made at this time.

Physical Examination.—The patient was stout and healthy looking and did not have any difficulty in standing or in gait. She held her head slightly tilted to the right, with the left shoulder somewhat raised. Although the strength of both the upper and the lower limbs was fairly good, the left upper and lower extremities were not as strong as the right, and the diminution in power was most distinct in the upper limb. In using her left hand she was distinctly clumsy, but it was uncertain whether or not the clumsiness was due to the distinct diminution in muscular power which existed. There was a slight atrophy of the intrinsic muscles of the left hand.

The tendon reflexes of the upper limbs were slightly hyperactive, but there was no difference between the two sides. The tendon reflexes in the left lower extremity were definitely more active than those of the right, with a fairly sustained patellar and ankle clonus, Babinski and Oppenheim signs were present on the left.

Cranial Nerves: The fundi were normal; the pupils were equal and reacted promptly to light and in accommodation. There was slight ptosis on the left and a few nystagmoid jerks when the patient looked to the left.

The sensory examination (fig. 1) showed that tactile and "deep" sensibilities were not affected, but that there was a slight but distinct diminution of pain and temperature sensibility on the right side of the body to the level of the third thoracic dermatome.

The spinal manometric test demonstrated a partial subarachnoid block. On x-ray examination made after the injection of a small amount of iodized oil 40 per cent by cisternal puncture, a few globules were arrested at the level of the second cervical vertebra, while the greater part of the oil promptly fell to the bottom of the vertebral canal. At the time of the puncture, Dr. Globus felt some resistance to the needle and therefore little iodized oil was injected. The spinal fluid was light yellow; the Wassermann test was negative; the fluid showed 20 cells to the cubic millimeter and the globulin was slightly increased.

Comment.—The history given by the patient and the results of examinations and tests indicated that she was suffering from a high compression of the spinal cord, probably due to an extramedullary neoplasm. It was clear that the growth lay on the left and probable that it was ventral or ventrolateral to the upper cervical segments. If a little more importance had been attached to the history of persistent headaches and to the slight ptosis and slight nystagmus, a diagnosis of a tumor which had only secondarily extended into the uppermost part of the vertebral canal might have been suggested.

Course.—On Oct. 25, 1927, the patient was operated on by one of us (Dr. Elsberg). The arches of the upper three cervical vertebrae were first

removed, and the dura was incised without injury of the arachnoid. To the left of the first and second cervical segments, the lower end of a brownish red tumor was seen, over which the second cervical root was tightly stretched (fig. 2). The growth lay ventrolaterally and evidently extended upward through the foramen magnum into the posterior cranial fossa. A suboccipital craniotomy was then performed, with removal of bone through the margin of the foramen magnum. The incision in the dura was enlarged upward in the shape of a V, so that the mesial parts of both cerebellar lobes were exposed. Above and to the left of the tumor was seen the lower part of the left cerebellar lobe; mesially, the arachnoid of the cisterna magna was seen.

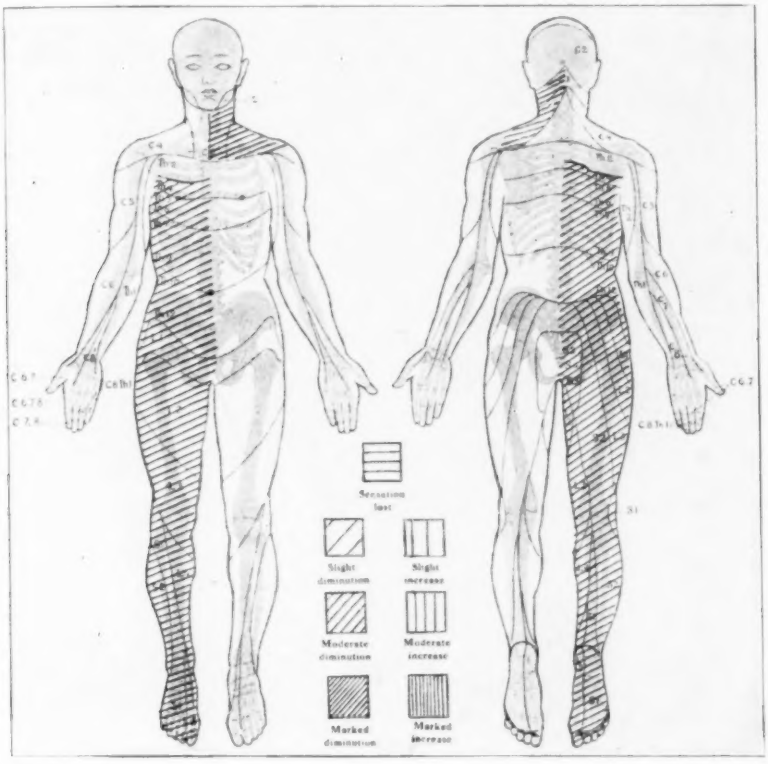

Fig. 1.—Sensory disturbances on Oct. 20, 1927, in patient R. H., who had an extramedullary tumor in front of the upper cervical cord and medulla.

The growth extended to the right in front of both the medulla oblongata and the upper cervical segments (fig 3). The arachnoid, which covered the lower part of the tumor, was split and an attempt made to draw the second cervical root away from the tumor. This was found to be impossible, and the root was therefore divided.

The tumor was slowly separated from the anterior surface of the medulla and cord and was gradually drawn to the left by means of a traction suture passed through the growth, after more of the laminae of the upper cervical vertebrae on the left side had been removed. As it was impossible to deliver the growth

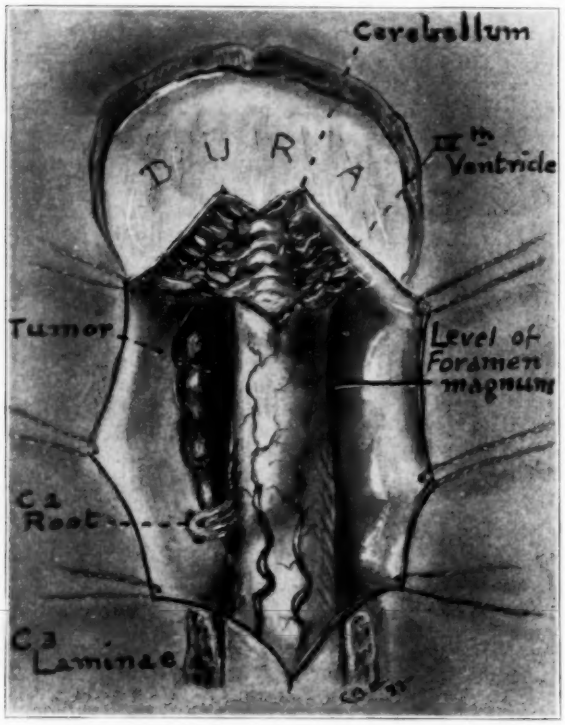

Fig. 2.—The tumor exposed at operation.

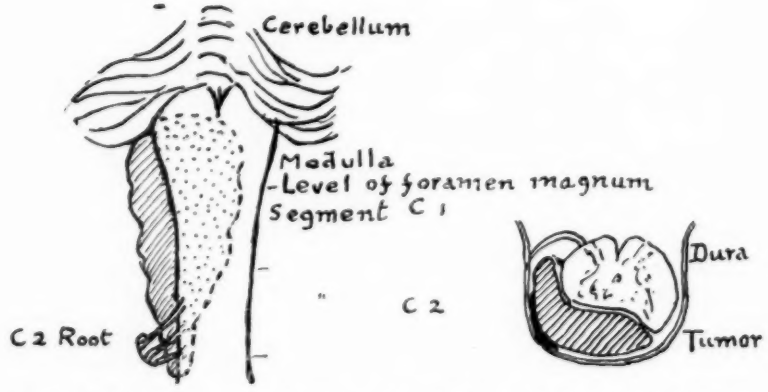

Fig. 3.—The position of the tumor with relation to the upper cervical segment and medulla (diagrammatic sketch made after the operation).

the most external part was excised, giving more room for lateral dislocation of the remainder. One adhesion after another was gently divided, the slightest oozing of blood in front of the medulla being controlled by means of pledgets of cotton soaked in epinephrine solution. Several times during the manipulations, there was a momentary cessation of respiration followed by a deep inspiratory movement.

Finally, the growth was freed on all sides and drawn to the left and removed, leaving a visible deep depression on the anterior surface of the medulla and upper cervical segments of the cord. In order to give support to these structures, several pieces of muscle were inserted into the tumor bed in front of the medulla and cord. Careful toilet of the wound was performed, with control of every trace of bleeding; suture of the dura, muscles, fascia and skin.

The operation lasted five hours, but the patient's condition was good at its close. There was no embarrassment of breathing, and the pulse rate and quality were satisfactory.

Fig. 4.—The tumor removed at operation.

Convalescence was uneventful. The patient improved rapidly and was discharged from the hospital forty days after the operation. When last seen she was free from all symptoms or signs of neurologic disturbance.

Pathology.—The tumor was a typical meningeal fibroblastoma (endothelioma). It measured 4.5 by 3 by 2.5 cm., and was well encapsulated (fig. 4).

The clinical and operative experience described led us to restudy the histories of our patients with tumors high in the cervical cord in order to learn whether it is possible to distinguish between growths that originate above the foramen magnum and grow downward into the vertebral canal and those that primarily compress the spinal cord and secondarily extend upward into the cranial fossa.[1] Furthermore, we

1. Tumors that arise in the posterior cranial fossa, even though they extend into the vertebral canal are in a strict sense tumors of the brain, but in the cases here considered, the symptoms are predominantly spinal and from the clinical standpoint they are considered as tumors of the spinal cord.

attempted to determine whether it is possible to distinguish between growths which are located entirely in the upper part of the vertebral canal and those that have extended upward through the foramen magnum into the posterior cranial fossa.

SOME CLINICAL FEATURES OF TUMORS HIGH IN THE CERVICAL CORD

On account of the relatively large size of the vertebral canal in the cervical region, extramedullary new growths in that location may reach a considerable size before marked signs of compression of the spinal cord occur. Radicular pain and hyperalgesia, in one or several cervical dermatomic areas, are usually prominent symptoms.

Aside from the actual level signs of tumors of the spinal cord which compress the uppermost cervical segments, there are some subjective and some objective disturbances which are worthy of special mention.

1. A fixed position of the head occurs frequently in persons with high cervical tumors—whether they project through the foramen magum or not. The head may be held bent to one or the other side, or the entire neck may be held rigidly on account of pain on movement. Rigidity of the cervical spine is not as frequent in new growths below the level of the sixth cervical segment as it is in compression of the cord above that level. As table 1 demonstrates, rigidity of the neck occurred: in five of seven patients with tumors in the upper cervical vertebral canal which extended through the foramen magnum; in two patients with compression of the spinal cord above the sixth cervical segment; in two of nine patients with tumors which involved the cord somewhere between the fifth and the eighth cervical segments. Thus, the head was held in a fixed position in seven of nine patients with high cervical growths as compared with two of nine patients with growths below the level of the fifth cervical segment.

2. Unless the signs of compression of the cord are far advanced, tactile sensibility may be little or not at all involved, so that the sensory disturbances are dissociated and make one think of an intramedullary disease. Thus, in four of nine patients with compression of one or more of the five upper cervical segments, the lightest touch with cotton wool was felt over the entire body below the level of the lesion, although the ability to recognize pain, warmth and cold was markedly affected. This surprisingly complete preservation of tactile sensibility, to which attention has been previously called by one of us (E.), is of considerable interest. It seems to indicate that in the uppermost part of the spinal cord either the pathways for touch travel in parts of the cord far separated from other forms of sensibility, that the nerve fibers which

transmit this modality of cutaneous sensibility are resistant to pressure, or that tactile sensibility can pass up the cord by one of a number of pathways.

3. When carefully questioned, patients with high cervical compression frequently complain of a feeling of intense cold in one or both lower limbs. They characterize this sensation as "icy" or freezing, and when the intense cold sensation is felt in only one lower extremity, it is most often the limb contralateral to the side of the tumor. We have not found this symptom in any tumors but those high in the cervical cord.

4. Atrophy of the muscles of one or both forearms and of the intrinsic muscles of the hands is frequent, not only in tumors which involve the lower half of the cervical cord but in those above the fourth cervical segment. This fact was first pointed out by Oppenheim, and cases have been reported by Oppenheim, Henneberg, Söderbergh, us

TABLE 1.—*Data of High Cervical Tumors*

Segment Level of Tumor	Extra-medullary	Intra-medullary	Extra-dural	Fixed Position of Head or Rigidity of Cervical Spine	
				Present	Not Present
First, second and third cervical segments and extending above the foramen magnum	6	1	0	5	2
Above sixth cervical segment	1	1	0	2	0
Below fifth and above seventh cervical segment	4	1	3	2	6
From sixth to eighth cervical segment	1	1	1	0	3
Total	12	4	4	9	11

and others. It is noteworthy that the wasting involves muscles the anterior gray horn cells of which are supposed to lie in segments below the part of the cord that is compressed.

For the differentiation between high cervical tumors below the foramen magnum and those that in addition extend upward into the posterior cranial fossa, there are few symptoms or signs that are absolutely reliable. Signs of cerebellar disturbance or of involvement of the cranial nerves are usually wanting or are not well marked, and unless the tumor in the posterior cranial fossa is large and the projection of it into the vertebral canal of insufficient size to compress the segments of the cervical cord, are always overshadowed by the symptoms and signs of the lesion of the spinal cord.

In two of our patients (cases 5 and 6 in table 2) a history of headache, pain in the occipital region, preceded by several years the appearance of symptoms of involvement of the spinal cord. In both of these patients, the larger part of the tumor lay above the level of the foramen

TABLE 2.—*Some Features of Tumors which Lay in Both the Vertebral Canal and the Posterior Cranial Fossa*

Case	Nature of Tumor	Location	First Symptom	Cranial Nerve Disturbances	Rigidity of Cervical Spine	Cerebellar Disturbances	Sensory and Motor Disturbances	Comment
1. N. I.	Extramedullary dermoid	On posterior surface of first and second cervical segments and extending 2 cm. above foramen magnum (fig. 5)	Pain in right side of neck	None	Marked	None	Marked in all limbs and trunk	Laminectomy and suboccipital craniotomy; tumor removed; recovery
2. M. S. H.	Extramedullary sarcoma	On posterior surface of first to fourth cervical segment and extending 1 cm. above foramen magnum	Pain in one shoulder	Nystagmus; slight facial weakness	Marked	None	Marked in entire body	Laminectomy; tumor removed; recovery
3. M. H.	Aneurysm of right vertebral artery	On ventral surface of medulla and first, second and third cervical segments (fig. 6)	Pain in back of neck	Slight disturbance of trigeminus—motor and sensory	Marked	None	Advanced over body and limbs	Laminectomy; died two days after exploratory operation
4. M. S. H.	Extramedullary meningeal fibroblastoma (endothelioma)	Dorsolateral to first and second cervical segments and extending 1 cm. above foramen magnum (fig. 7)	Numbness and stiffness of left hand	Slight left facial weakness	Distinct	None	Tactile sensation, normal; pain and temperature markedly involved; marked motor signs	Laminectomy, first to fourth cervical segments; tumor removed; recovery
5. M. S. H.	Extramedullary meningeal fibroblastoma (endothelioma)	Ventrolateral to first and second cervical segments with large tumor in posterior cranial fossa (fig. 8)	Occipital headache; dyspnea on exertion	Left pupil > right; left palpebral fissure > right	None	None	Tactile sensation, normal; pain and temperature not much involved	Laminectomy; tumor removed; death; at postmortem, tumor in posterior fossa with downward extension into vertebral canal
6. M. S. H.	Extramedullary meningeal fibroblastoma (endothelioma)	Ventrolateral to medulla oblongata and upper three cervical segments of cord	Headache, pain in back of head and down left side of neck	Slight ptosis on left; slight nystagmus to left	Marked	None	Tactile sensation, normal; pain and temperature diminished; motor disturbance not marked	Laminectomy and suboccipital craniotomy; tumor removed; recovery

magnum and was probably the primary part of the growth (figs. 3 and 8). Notwithstanding this, the signs of disturbed function were almost entirely limited to the spinal cord. In these two patients, a diagnosis of tumor both above and below the foramen magnum should have been made.

On the other hand, when the first symptoms are those referable to the upper part of the vertebral canal—to the neck, the top of the shoulder or to a part of one upper limb—it is more probable, as in cases 1, 2, 3

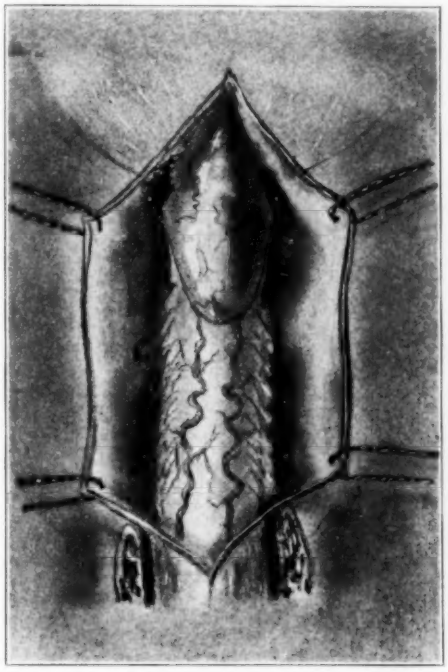

Fig. 5.—Extramedullary dermoid cyst on the posterior surface of the upper cervical segments and medulla in patient R. G.

and 4 of our series, that the growth began in the vertebral canal and extended upward through the foramen magnum (figs. 5, 6 and 7).

If carefully looked for, slight evidence of a lesion of the posterior fossa—nystagmoid jerks on lateral gaze, slight facial weakness, an ébauche of deviation of the tongue when protruded, perhaps slight diminution in the sensibility of one or both corneas—will be found in many tumors that are high in the cervical cord. These disturbances are less frequent in the cases in which the growth is limited to the vertebral canal below the foramen magnum, as compared with the growths which are both supraforaminal and infraforaminal (table 2).

SURGICAL TREATMENT

For the exposure and removal of tumors which lie both above the foramen magnum, in the posterior cranial fossa, and below it in the vertebral canal, a bilateral removal of the arches of the upper cervical vertebrae is usually necessary. If the growth extends only a small distance above the margin of the foramen, it may be possible to draw it downward; a small part of the margin of the foramen may have to be removed by a rongeur, or, finally, more or less of the occipital

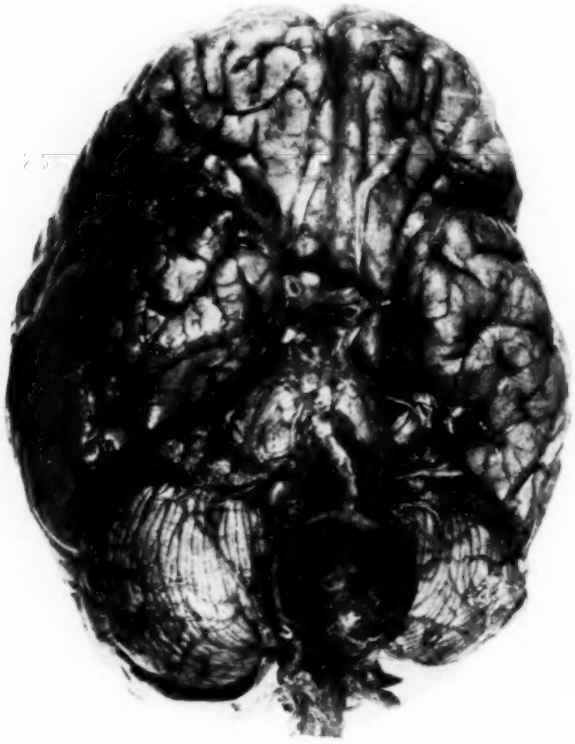

Fig. 6.—Aneurysm of the right vertebral artery compressing the medulla and upper cervical cord in patient M. H. (from Elsberg: Tumors of the Spinal Cord, 1925, p. 300).

bone must be removed, so an adequate exposure of the posterior cranial fossa may be obtained. The operation should always begin with laminectomy, and, if required, the midline incision should be enlarged upward to the external occipital protuberance and the bone removed in the same way as is done for a cerebellar exposure through a midline incision. In patients with a short neck, in order to expose adequately the laminae of the first three cervical vertebrae, it may be necessary to

make the first incision from the external occipital protuberance to the middle of the cervical spine, even though the muscles are not separated from the bone in the suboccipital region.

After the dura has been incised and the tumor has been exposed, the surgeon must make certain that the upper limits of the growth are actually in plain view and that the tumor does not extend further upward into the posterior cranial fossa. Otherwise, and especially if the part of the growth at the margin of the foramen magnum is thin,

Fig. 7.—Extramedullary meningeal fibroblastoma dorsolateral to the first and second cervical segments and extending above the foramen magnum in patient R. H.

the spinal part may be removed in the belief that there is no extension into the posterior cranial fossa, and the part of the growth in the posterior cranial fossa may be left. This actually occurred in case 4 of our series, in which the spinal part of the tumor was connected by only a thin band of tissue with the main intracranial growth. The patient was operated on before we had understood this possibility and before we had fully realized that in every instance a part of the growth

may be in the posterior cranial fossa, although prominent symptoms or signs of a lesion of the posterior fossa are not present.

When the incision in the dura is enlarged upward above the foramen magnum, in order to avoid the sinus rectus it is advisable either to divide the membrane along one side of the median line or to turn up a V-shaped flap of the dura so that the entire incision in the dura is Y-shaped.

The actual removal of the growth, if it is extramedullary, is always difficult and time consuming, and gentleness of manipulation and the most scrupulous control of even slight bleeding are necessary. If the tumor lies outside the arachnoid, every effort must be made to preserve

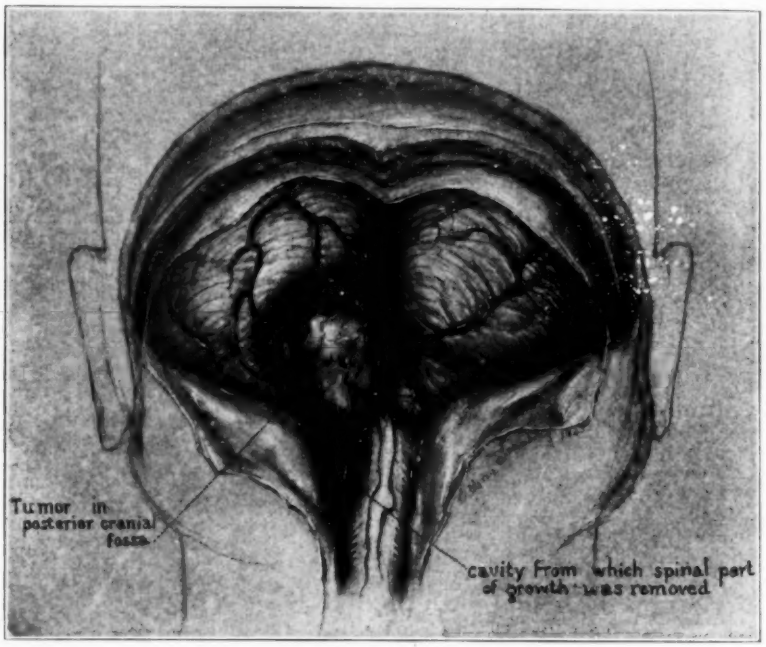

Fig. 8.—Extramedullary meningeal fibroblastoma ventrolateral to the first and second cervical segments, a downward extension of a large tumor in the posterior cranial fossa in patient J. R. (from Tilney and Elsberg: Sensory Disturbances in Tumors of Cervical Spinal Cord, Arch. Neurol. & Psychiat. **15**:444 [April] 1926).

the walls of the cisterna magna, the fluid in it being evacuated either by puncture of the cistern with a fine needle, or by incision of the arachnoid in the vertebral canal and drainage of the cisterna by this means.

CONCLUSIONS

1. In every patient with signs and symptoms of compression of the uppermost segments of the spinal cord, the possibility that the growth may involve both the vertebral canal and the posterior cranial fossa must be kept in mind.

2. If the history obtained from the patient contains statements of headache or pain in the head which preceded, by a definite period, the signs and symptoms of compression high in the cervical cord, it is probable that the growth is located in both the posterior cranial fossa and the vertebral canal, and also that the growth originated in the cranial chamber and extended into the vertebral canal through the foramen magnum.

3. The presence of nystagmus, of weakness of one side of the face or of sensory disturbances of the cornea or within the remaining area of distribution of the trigeminal nerve on one or the other side make it probable, but not certain, that the growth involves not only the upper cervical segments but also the posterior cranial fossa.

4. If the early symptoms began in the neck, shoulder or an upper extremity, the new growth was primary within the vertebral canal even though it may have finally involved the posterior cranial fossa and may have given rise to disturbances of some of the cranial nerves.

5. The absence of disturbances of the cranial nerves does not negate the possibility that part of the growth lies in the posterior fossa, and the presence of such signs is not certain evidence that the growth extends through the foramen magnum into the cranial cavity.

INCISURA OF THE CRUS DUE TO CONTRALATERAL BRAIN TUMOR *

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AND
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The diagnosis of organic nervous diseases rests on a foundation built largely by anatomists, pathologists and physiologists. For this reason, it compares favorably in accuracy with diagnoses in other fields of medicine. In the localization of tumor of the brain, however, astonishing difficulties are often encountered. Thus, Magnan [1] (1878) reported a case of tumor and softening in the region of the left rolandic fissure, in which there were convulsive movements on the left side. The patient also had dementia paralytica and the marked meningo-encephalitis on the right side explained the convulsions on the left. Tucker [2] (1917) reported a case (case 4) of tumor of the left temporal lobe in which left hemiplegia was also present. Massive hemorrhage was noted in the right subcortical area. Meyer [3] (1920) reported a case in which a supratentorial tumor had produced such marked herniation that the tentorial edge impinged on the right posterior cerebral artery, thus furnishing the basis of hemianopia. We correctly localized a small endothelioma in the sensorimotor area, but missed an enormous glioma in the opposite hemisphere. These explanations were eminently satisfactory, but satisfactory explanations are not always forthcoming.[4]

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* From the Sections on Pathologic Anatomy and Clinical Neurology of the Mayo Clinic.

* Read at the Fifty-Fourth Annual Meeting of the American Neurological Association, Wasington, D. C., May 1-3, 1928.

1. Magnan: General Paralysis and Cerebral Tumour with Atrophy of the Ascending Parietal Convolution of the Left Hemisphere—no Paralysis on Right—Convulsions on Left, Brain **1**:562, 1878-1879.

2. Tucker, B. R.: A Study of Fifteen Cases of Brain Tumor of Obscure Localization, Internat. Clin. **4**:194, 1917.

3. Meyer, Adolf: Herniation of the Brain, Arch. Neurol. & Psychiat. **4**:387 (Oct.) 1920.

4. Since we completed our review of the literature in preparation for this report, a recent and noteworthy contribution by Groeneveld and Schaltenbrand came to our notice. These authors reported a case of tumor of the brain in a man, aged 43, who had had jacksonian convulsions and impairment of sensation on the right side, spastic hemiparesis on the left side, slowness in thinking and euphoria. At necropsy, a tumor was found over the left sylvian fissure, which had displaced the brain toward the right, resulting in longitudinal stretching of

REPORT OF CASE

Our interest in this subject sprang from the shadow of a baneful experience in the following case: [5]

A man, aged 47, was brought to the clinic because of mental deterioration and convulsions. The convulsions had begun six months before examination and were always more violent on the left side than on the right. Subsequently, occipital and frontal headaches appeared, incontinence developed and the patient became much confused.

Neurologic examination showed bilateral choked disks of 3 diopters and slight diminution of hearing on the left. The speed of movement was slightly diminished in the left upper extremity and rather less so on the right. The gait was moderately spastic on the left and slightly so on the right. A strongly positive Babinski phenomenon was present on the left. The outstanding features of the mental condition were marked slowness in cerebration and a tendency to fill in the narrative history of past events from imagination, in a manner resembling Korsakoff's psychosis. We believed that we were dealing with a tumor of the frontal lobe which impinged on the temporal lobe, as suggested by the convulsions. The evidence of disturbance of the pyramidal tract, chiefly on the left side of the body, led us to make a diagnosis of tumor of the right frontal and temporal lobes.

At necropsy, a tumor was found, not on the right side of the brain, but in the left frontotemporal area (fig. 1). In searching for an explanation of the discrepancy between the symptoms and the lesion, it was noted that because of the large size of the tumor, the brain, including the brain stem, was displaced to the right in such a manner that the right crus cerebri was brought hard against the free edge of the tentorium. This edge caused a distinct indentation in the crus (fig. 2). It was thought that this notching of the crus might be sufficient to interrupt some of the right corticospinal fibers and cause the positive Babinski sign on the left (fig. 3).

Mistakes of this kind are not rare, but few reports can be found. Flatau [6] reported the case of a man who had, among other symptoms, left hemiplegia, and who had been treated by irradiation for a tumor of the right frontal. Necropsy disclosed a tumor in the left frontal lobe. Purves Stewart [7] included a similar case (case 10) in his book, "Intracranial Tumors and Some Errors in Their Diagnosis."

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the internal capsule and peduncle and the production of a notch in the pes pedunculi by the free edge of the tentorium on this side. They concluded that this notch and pressure on the posterior margin of the petrous part of the temporal bone was responsible for the left hemiparesis. Secondary degeneration was not found. Groeneveld, A., and Schaltenbrand, G.: Ein Fall von Duraendotheliom über der Grosshirnhemisphäre mit einer bemerkenswerten Komplikation: Läsion des gekreuzten Pes pedunculi durch Druck auf den Rand des Tentoriums, Deutsche Ztschr. f. Nervenh. **117**:32, 1927.

5. Kernohan, J. W., and Woltman, H. W.: Incisura of the Crus Due to Contralateral Brain Tumor, Proc. Staff Meetings Mayo Clinic **3**:69, 1928.

6. Flatau, E.: De la radiothérapie des tumeurs du cerveau et de la moelle, Rev. neurol. **31**:23, 1924.

7. Stewart, J. P.: Intracranial Tumors and Some Errors in Their Diagnosis, London, Milford, 1927, p. 206.

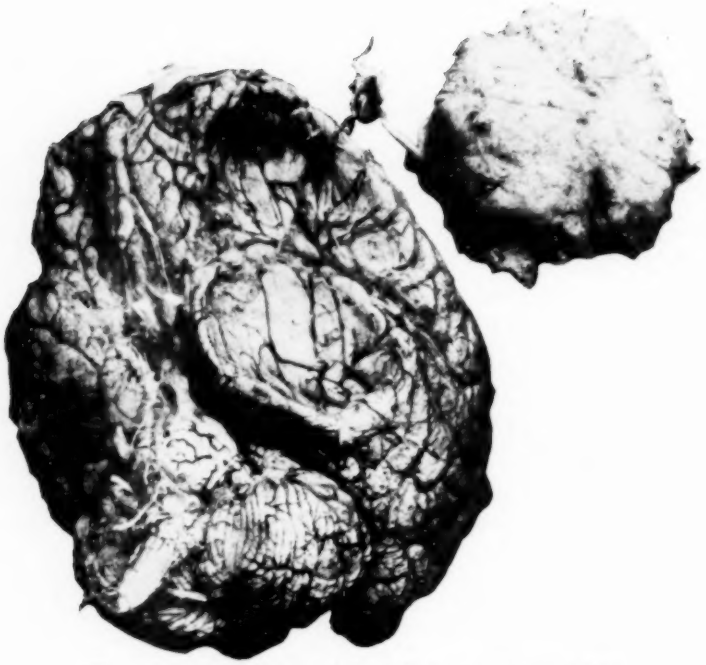

Fig. 1.—Endothelioma of the left frontotemporal lobe.

Fig. 2.—Right pes pedunculi showing notch, indicated with arrow. Blood vessels and pia mater not entirely removed. Same case as in figure 1. The groove in the left uncinate gyrus is indicated by two arrows.

The cause of such errors appears to be primarily mechanical. Most tumors, to gain quarters for themselves, push the substance of the brain into peculiarly partitioned chambers of limited space. This often results in producing direct or indirect injury to distant structures, and the pyramidal tract of the opposite side frequently suffers. We shall not discuss this phase in detail, as it has been done excellently in a recent report by Gould.[8] Hydrocephalus, or increased pressure alone, is often noted in the ventricle opposite a supratentorial tumor, as brought out by

Fig. 3.—Longitudinal section through pes pedunculi. Same case as in figures 1 and 2. The site of compression with the myelin destruction is shown. Weigert's myelin sheath stain.

Elsberg and Gilbert (quoted by Gould). Presumably, this may be the site of injury. Another possible site of injury to the contralateral pyramidal tract is the pons, which, in infratentorial tumors, is frequently distorted. Gould, in discussing infratentorial tumors, stresses the factor of pressure of the medulla on the free rim of the foramen magnum.

8. Gould, E. M.: Tumors of the Posterior Cranial Fossa: Homolateral and Contralateral Pyramidal Tract, Arch. Neurol. & Psychiat. **19**:509 (March) 1928.

Whether or not lateral displacement of the brain stem by tumor, either supratentorial or infratentorial, could be sufficiently great to result in a notching of the contralateral crus by the free edge of the tentorium and thus produce pyramidal signs on the same side as the tumor, and, if so, whether it occurs with sufficient frequency to be worthy of note, were the questions that stimulated our interest. Obviously, we are dealing with a number of possibilities.

The problem was approached from the pathologic and clinical sides independently. Two hundred and seventy-six brains with tumors,

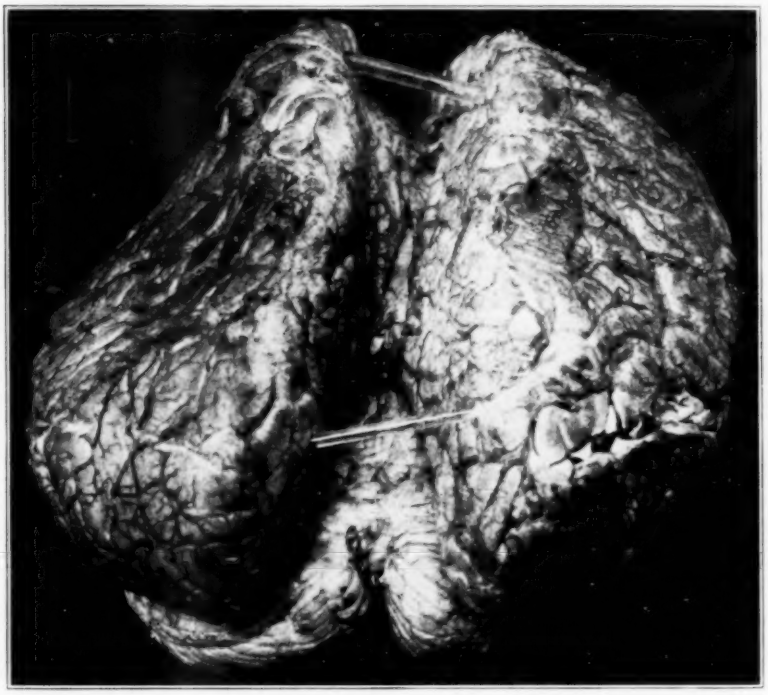

Fig. 4.—Marked compression of the left cerebral hemisphere by subdural hematoma. Herniation through the falx cerebri is shown.

obtained at necropsy, were studied. Specimens with metastatic and median line tumors were excluded, in order to reduce as much as we could the possibility of direct injury to the opposite pyramidal tract by the tumor itself. Of the specimens that remained, thirty-four (12 per cent) were found with various degrees of notching, always on the side opposite the tumor. Twenty-nine of these were supratentorial, of which five were extramedullary, and five were infratentorial, all of which were extramedullary. It will appear that this bears out Gould's contention that relative hyperreflexia on the same side as the tumor suggests extra-

Fig. 5.—Right peduncle; same case as in figure 4; groove indicated by arrow.

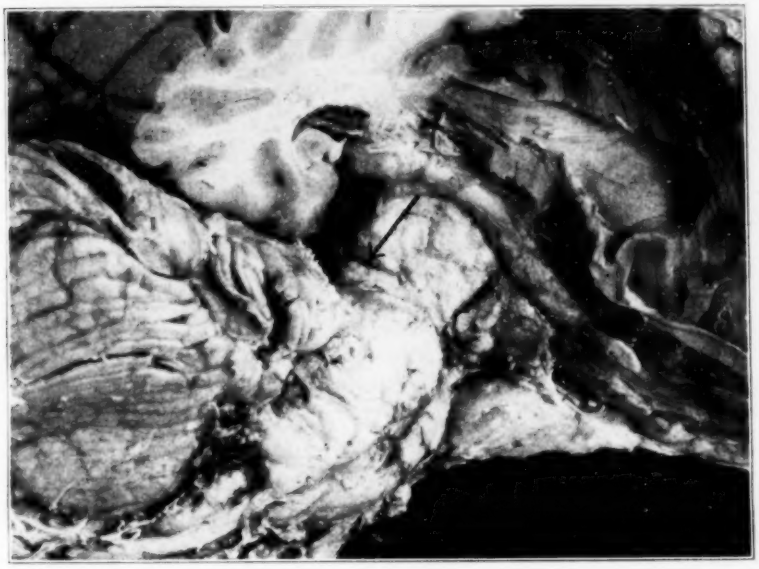

Fig. 6.—Groove in right peduncle indicated by arrow. (Case of abscess in left parietotemporal lobe.)

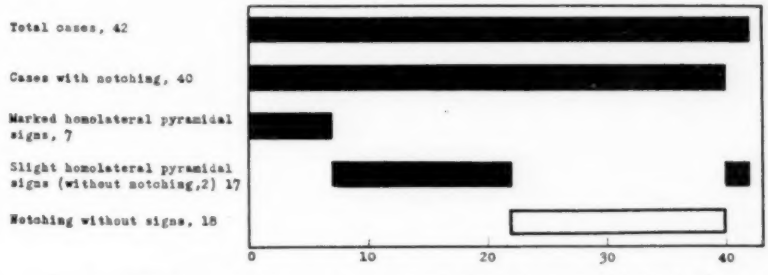

Fig. 7.—Incisura of the crus due to contralateral tumor of the brain.

cerebellar rather than intracerebellar disease. Notches were also found in one case of chronic subdural hematoma (figs. 4 and 5) and in five cases of abscess (fig. 6), all supratentorial, bringing the total number of cases with notching to forty (fig. 7).

The histories corresponding to the 276 specimens of tumor, excluding those with metastatic and median line involvement, were then reviewed, with the purpose of selecting those which showed more active tendon reflexes or abnormal plantar responses on the homolateral side. Twenty-four cases filled these requirements.

The cases selected on the pathologic and clinical criteria were then analyzed. It was discovered that two other cases similar to the one reported had been observed, in which the tumor was localized on the wrong side because of hemiparesis on the same side as the tumor. In both of these there was distinct notching of the crus. We had been saved from making this error in four other cases, in three of which partial hemiplegia was present on the side of the tumor. Error was avoided by disregarding the evidence of homolateral involvement of the pyramidal tract, in view of aphasia in the first case, of hemianopia in the second, of a mass on the external aspect of the skull in the third, and a history of the patient's having dragged the opposite leg in the fourth. There was a contralateral notching of the crus in all of these.

In fifteen additional cases, five of which were angle tumors, there was likewise evidence of homolateral involvement of the pyramidal tract. This, however, did not interfere with the making of a diagnosis. The notching found in the opposite crus, we believe, could have explained the signs of the homolateral pyramidal tract in all of these.

Two of the twenty-four cases of homolateral involvement of the pyramidal tract remained. One of these was a glioma of the right cerebellar lobe which was accompanied by well marked hydrocephalus; the other was a case of glioma of the left frontal lobe in association with marked herniation of the medulla through the foramen magnum. Incisura was not found in either case. The hydrocephalus and the herniation may have explained the clinical signs. It is also possible that compression without actual destruction by pressure from the tentorial edge may have caused blocking of the corticospinal pathway.

In eighteen cases more or less notching was found; in these a survey of the corresponding histories did not disclose the presence of homolateral signs of the pyramidal tract on which we based our selection. In five of these cases, however, tendon reflexes were active on the same side as the lesion. For the remaining discrepancies, we do not have an adequate explanation.

Fig. 8.—Endothelioma of the left frontal lobe.

Fig. 9.—Right peduncle; same case as in figure 8; notch in peduncle just above upper edge of pons is indicated by an arrow.

DESCRIPTION OF THE GROOVES

The tumor was often large enough to displace the brain toward the opposite side and also to cause herniation through the tentorium. Such herniation and displacement may be evidenced by a groove sweeping over the uncinate gyrus on the side of the tumor. On the opposite side the groove may be absent; it may involve only a small portion of the uncinate gyrus, or it may be found to cut across the crus cerebri. To demonstrate the notching, it may be necessary to strip off the arachnoid

Fig. 10.—Groove in peduncle without destruction of myelin sheaths. Weigert's myelin sheath stain; × 12.

and blood vessels or even to take sections across the suspected area. Although blood vessels may occupy grooves of their own, they were evidently not responsible for the notching under consideration. The notches in the crus, produced by pressure of the free edge of the tentorium, are usually found close to the entrance of the crus into the pons, although sometimes they may be as far as 1 cm. above this level. As a rule, the most convex portion of the pes is involved, but occasionally it may be more posterior. The deepest portion of the groove is at the

center; it is less deep anteriorly and posteriorly. The average length of the notch is about 1.5 cm. These grooves vary in gross appearance; they are sometimes shallow with little tissue destruction and sometimes deep with tissue destruction and signs of old or recent petechial hemorrhages.

Fig. 11.—Site of incisura with myelin destruction beneath. Weigert's myelin sheath stain; × 12.

The corticospinal fibers appeared to be intact between the precentral gyrus and the notch.

Sections were taken at right angles to the groove across the pons, so as to include the corticospinal fibers and also at the decussation of the

pyramidal tracts in the medulla oblongata. Weigert's myelin sheath stain and Marchi's stain were used on each, and general stains at the site of the incisura.

Weigert's myelin sheath stains showed, in most cases, definite destruction of tissue, sometimes only superficially, but sometimes down to the

Fig. 12.—Site of incisura with more marked myelin destruction. Weigert's myelin sheath stain; × 12.

substantia nigra. Occasionally (fig. 10), there was definite compression of the tissue without destruction of the myelin sheaths. Only rarely was there any sign of descending degeneration, as demonstrated by the Weigert stain, either at the incisura, in the pons or in the medulla

Fig. 13.—Site of incisura with more extensive myelin destruction even down to the substantia nigra. Weigert's myelin sheath stain; × 12.

Fig. 14.—Marchi preparation showing active destruction of myelin below site of incisura; × 75.

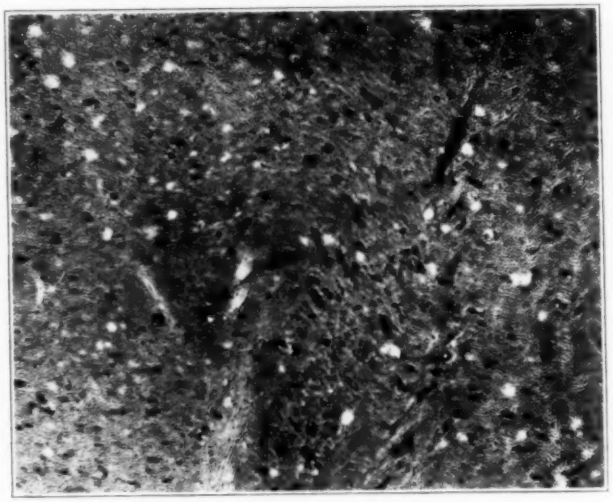

Fig. 15.—Marchi preparation of medulla oblongata, showing degeneration of the corticospinal fibers at the level of the decussation; × 75.

oblongata. Scharlach R stains rarely revealed free fat at the site of the lesion. The Marchi stain, however, did show, in some instances, varying degrees of degeneration below the notch and also in the pyramidal tract in the medulla oblongata. In none of the cases in which sections were taken was there degeneration above the incisura.

The Orlandi stain of the axis cylinders showed that most of the axis cylinders at the site of compression were not destroyed, although some did show evidence of degeneration and were fragmented and swollen below the site of the lesion. From this it seemed that the compression, while it frequently caused local destruction of the myelin, did not, as a rule, interrupt all the corresponding axis cylinders. That some were involved in a few cases was evidenced by the descending degeneration seen in the Marchi preparations.

The general stains showed, in most cases, changes in the glia cells and other evidences of a definite antemortem reaction, which also served to show, if further evidence was needed, that the notching was neither an artefact nor postmortem trauma. In one case only was there bilateral notching of the pes pedunculi, and this was where a large pituitary tumor had dislocated the entire brain stem backward, causing its impingement against the converging edges of the tentorium. Each pes was equally involved.

COMMENT

In presenting this material, we intentionally limit ourselves to the presentation of data with reference to only one of the possible causes of the homolateral involvement of the pyramidal tract noted in some cases of tumor of the brain. It is obviously impossible to ascribe to each of the mechanisms that may be involved its just and proper weight. Notching of the crus cerebri by the free margin of the tentorium could, we believe, explain the homolateral signs of the pyramidal tract noted in most of our cases.

ABSTRACT OF DISCUSSION

Dr. Riley, New York: Was the mesencephalic region investigated in cases in which the patients did not show homolateral signs and is there a possibility of these markings being due to the superior cerebellar or the anterior inferior cerebellar artery?

Dr. James W. Kernohan: It was necessary to remove the posterior cerebral and other subarachnoid arteries in this region to see the notch, which was not necessarily directly underneath. The grooves did not seem to be the result of arterial compression and in these cases none of the vessels was thrombosed. The mesencephalic region was investigated in all cases.

INTRA-UTERINE POLIOMYELITIS

REPORT OF A CASE IN WHICH A RECRUDESCENCE OF SYMPTOMS OCCURRED AFTER FIFTY YEARS *

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The transmission of various infectious diseases, such as variola, erysipelas, diphtheria and tuberculosis, from the mother to the fetus in utero has been reported a number of times. That epidemic encephalitis can be so transmitted seems probable. Achard and Netter [1] cited two cases in which the mothers had the disease. One child was markedly somnolent and had retention of urine for several days after birth; the other had myoclonia and hemorrhagic papules. The authors concluded by stating that "in encephalitis, as in other maternal infections, the fetus may be infected through the placenta but this does not invariably occur." Mercier, Andrieux and Bonnaud [2] reported the case of a woman who contracted the disease in the eighth month of pregnancy and died from it eighteen days after delivery. Two weeks after birth, the child developed myoclonic movements of the head and arms, retraction of the head, stiffening of the limbs and slight twitchings of the muscles about the mouth and upper limbs. From these he gradually recovered until in three months he was apparently well except that at times a slight convergent strabismus was present. These authors stated that the symptoms in the child resembled those in the mother, but were of a milder type. Marinesco [3] cited the case of a woman five months pregnant who developed encephalitis from which she died fifteen days later. Examination of the brain of the fetus showed slight changes which he stated were true lesions of encephalitis—the result of the virus being transmitted across the placenta and causing changes in the brain of the fetus. Two cases were reported by Jorge,[4] who gave references

* Submitted for publication, June 19, 1928.

* The patient was shown before the Philadelphia Neurological Society, March 27, 1918, and the paper read before the Philadelphia Neurological Society, April 27, 1928.

* From the Departments of Neurology and Neuropathology of the Philadelphia General Hospital.

1. Achard and Netter: À propos de la transmission placentaire de l'encéphalite léthargique, Bull. Acad. de méd., Paris **85**:645 (May 31) 1921.

2. Mercier, Andrieux and Bonnaud: Transmission placentaire de l'encéphalite épidemique, Bull. Acad. de méd., Paris **85**:625, 1921.

3. Marinesco: L'encéphalite épidemique dans la grossesse, Rev. neurol. **37**: 1055, 1921.

4. Jorge, Ricardo: L'encéphalite léthargique et la grossesse. (Transmission placentaire de la mère au foetus), Paris méd. **39**:453 (June 4) 1921.

to three others and stated that in Portugal, in 1920, reports of eight cases of placental transmission of encephalitis were collected. Levaditi, Harvier and Nicolau [5] transmitted the disease in rabbits from the mother to the fetus. An injection of an emulsion of fetal brain into another animal caused death in nine days, and typical lesions of encephalitis were found. No clinical symptoms were present. Injection of an emulsion of the liver did not cause symptoms. These authors concluded that this experiment shows that the virus of encephalitis crosses the placental filter to localize itself in the central nervous system of the fetus, even when the disease has not apparently been present in the mother. Encephalitis due to other infections may also be so caused.

As early as 1867, Virchow [6] reported the case of an infant who died six days after being born of an apparently healthy mother. In the brain and cord, lesions of an acute inflammatory nature were found. He concluded with the statement that "Both prenatal deaths and those occurring shortly after birth are due in large numbers to prenatal encephalitis and myelitis. It is conceivable that such encephalitic and myelitic affections are not always fatal. . . . . It is most probable that many cases of idiopathic and deuteropathic paralyses of the infant and many instances of idiocy can be traced back to such encephalitic changes."

Freud,[7] in 1897, wrote that all the diplegias which dated from birth really had their pathologic origin long before birth in intra-uterine life and that the universal degeneration of cortical cells points to the advent of a rapid degenerative change shortly before birth. In this connection, Madame Long-Landry [8] has referred to some interesting cases in which muscular rigidity was present from birth. In these, autopsies revealed various evidences of inflammation of the brain cortex and meninges. More recently, Collier [9] has stated that: "The essential anatomical cause of a diplegia is a primary degeneration of the cerebral neurons from causes which are at present elusive, with the exception of the rare cases in which syphilitic infection of the brain is certainly the provoking agent." He expressed the belief that there may be several causes, one of which may be toxic. Globus [10] reported the case of a child in whose

5. Levaditi, Harvier, and Nicolau: Transmission expérimentale du virus de l'encéphalite de la mère au foetus, Compt rend. Soc. de biol. **84**:957 (May 28) 1921.

6. Virchow: Congenital Encephalitis and Myelitis, Virchows Arch. f. path. Anat. **38**:129, 1867.

7. Freud: Die infantile Cerebellähmung, in Nothnagel: Specielle Pathologie und Therapie, Vienna, Hölder, 1897, vol. 9, pt. 2, no. 2.

8. Long-Landry: Le maladie du Little (Étude anatomique et pathogénique), Thèsis de Paris, 1911.

9. Collier: Pathogenesis of Cerebral Diplegia, Brain **47**:1, 1924.

10. Globus: A Contribution to the Histopathology of Porencephalus, Arch. Neurol. & Psychiat. **6**:652 (Dec.) 1921.

brain evidence of an inflammatory process (meningo-encephalitis) was found. He stated that "The extensive destruction of the cerebral cortex and eleven months of postnatal life not marred by any illness lead to the conclusion that the destructive process must have begun in the latter part of the intrauterine life period and remained active and slowly progressive after birth." The mother had not had any symptoms of illness. Patterson and Carmichael [11] described a family consisting of normal parents in whom the Wassermann reaction was negative and to whom twelve children were born; of these, ten died in early infancy. Autopsies in two—aged 3 days and 6 months, respectively—showed an inflammatory process at the base of the brain involving the meninges, an ischemic condition of the lenticular nucleus, maldevelopment and degeneration of the cortex, maldevelopment of the myelin formation and a perivascular degeneration of toxic origin. Plasma cells were not present. The authors concluded that the lesions were due to an infective organismal state of the base of the brain with consequent toxemia which affected chiefly the cells of the cortex; that this infection was of antenatal origin. They believed its source to be a severe endometritis from which the mother was suffering.

There seems to be good reason from the foregoing to believe that cerebral disease from various causes, some of which are either toxic or infectious, may occur in the fetus in utero, and that some cases of so-called Little's disease are so caused. The literature referring to disease of the spinal cord due to similar causes is not so large. Long-Landry [8] reported the following case, believed to be congenital, in which the lesions were confined to the spinal cord.

J. B. died at the age of 3 years and 11 months. The child was apparently normal until a few months old. At that time it was noted that the legs were greatly contracted; the lower limbs were atrophied, all reflexes were exaggerated, and there was a bilateral Babinski sign. The trunk, head and arms developed normally. Later, there were athetoid movements of the arms. Intelligence was normal. At the autopsy the brain was normal, grossly and microscopically. The medulla, and the cervical and upper dorsal cord were normal. In the lower dorsal cord two fusiform swellings were noted. One lay at the level of the eighth dorsal segment and the other at the level of the tenth, eleventh and twelfth dorsal segments. At these levels, section showed poor differentiation between the gray and the white matter. The morphology of the anterior and the posterior horns showed a change. The pia was thickened and opalescent, with the greatest changes in the posterior regions at the emergency of the roots. Microscopically, the meninges showed a meningitis, most marked around the roots and extending from the lower cervical region to the conus. Disseminated throughout the cord and most marked in the gray matter were areas of perivascular necrosis, often miliary. The

11. Patterson and Carmichael: A Form of Familial Cerebral Degeneration Chiefly Affecting the Lenticular Nucleus, Brain **47**:207, 1924.

crossed pyramidal and cerebellar tracts were most affected. The direct pyramidal tract was intact. There were abortive lesions in the medulla and the superior cervical cord.

It has been claimed, and the case of Globus [11] shows this to be true, that in intra-uterine infection the symptoms may not be apparent until several weeks after birth and may progress for some time after.

Dejerine [12] reported two cases in which the patients—believed to have Little's disease—were found after death to have lesions confined to the spinal cord. In the first, who died when 66 years of age, there was a transverse area of sclerosis in the third cervical segment. The blood vessels showed changes suggestive of syphilitic change. He considered it a case of myelomalacia due to syphilitic endarteritis developed during intra-uterine life. The second patient, who died when 44 years old, was born paralyzed and rigid in all four limbs and did not walk until 9 years old. The cord was smaller than normal, and the posterior part of each lateral column was composed of a sclerotic plaque. Between the first and second cervical roots in an area about 0.5 cm. in diameter was a destruction of the posterior horns with a sclerotic plaque. These plaques contained many blood vessels which showed periarteritis and endarteritis. Dejerine concluded that "Little's syndrome can be caused by a primary medullary lesion—a circumscribed lesion developed during intra-uterine life, of which the pathogenesis is unknown, although in this case, the hypothesis of a medullary intra-uterine infection seems very probable."

In 1894, Lamy [13] reported the case of a man, aged 43, who had had an atrophic paralysis of the right leg which had apparently been present since birth or at least from earliest childhood. In the first week of life he had had numerous convulsions. Microscopic examination showed evidence of cortical encephalitis on the left side and marked atrophy of the anterior horns in the lumbosacral region of the right side.

Batten,[14] in 1910, reported two cases, the first of which he regarded —both from the history and the results of microscopic examination of the cord—without doubt one of intra-uterine poliomyelitis. In the second, while undoubtedly a case of this disease, the evidence was not so clear as to its uterine origin. The author also mentioned a

12. Dejerine: Sur la rigidité spasmodique congénitale d'origine médullaire (syndrome de Little) par lesion médullaire en foyer développée pendant la vie intrauterine, Rev. neurol., 1903, p. 601; Deux cas de la rigidité spasmodique congénitale avec autopsie, Soc. de biol., 1897, p. 261.

13. Lamy: Sur un cas d'encéphalite corticale et de poliomyélite antérieure associée, Rev. neurol., 1894, part 2, p. 313.

14. Batten: Does Poliomyelitis Occur in Intra-Uterine Life? Brain **33**:149, 1910.

case reported by Fritsch,[15] in 1908, as being one of this nature. It did not come to autopsy, however, and was therefore regarded as doubtful.

The foregoing citations from the literature make it clear, I believe, that antenatal infection of the brain and cord can occur and that different forms of infection may so act.

REPORT OF CASE

In this connection, the following case is of interest.

Clinical History.—Oscar V., a newsdealer, aged 54, single, was admitted to the neurologic wards of the Philadelphia General Hospital in February, 1916. With the exception of brief intervals, he remained there until his death in March, 1925. His complaint was weakness of both legs, especially the right, and of the left arm and hand. He stated that he had been weak since birth and did not walk until he was 6 years old. Since then, he had walked with difficulty but without assistance. Until admission, he had made a living selling newspapers. His brother, an intelligent man, and a relative who is a physician stated that the patient had been as he was since birth and that he had not grown worse since that time. The only acute illness suffered from were measles, chickenpox and smallpox. When the mother was four months pregnant with the patient she had a severe fall, in consequence of which she was confined to bed for several weeks. He had indulged in alcoholic drinks to some extent, used tobacco, and denied ever having had sexual intercourse or any venereal disease. The Wassermann reaction was, however, positive in the cerebrospinal fluid on two occasions (March 8, 1916, and Aug. 20, 1917), and in the blood on one, these being all the tests made. Shortly before admission, he had fallen and fractured the left femur. Evidence of this had disappeared when he entered the hospital. The family history was unimportant.

Examination.—The man was small and walked without assistance but with effort, as talipes equinovarus of the right foot and valgus of the left were present. If he stood for any length of time, tremors of the left leg occurred. The pupils were irregular and equal and reacted to light and in convergence. At a later examination in September, 1920, Dr. Wilson noted that they were irregular, unequal and reacted poorly to light and in convergence. There was slight drooping of the left side of the face, and the teeth were shown better on the right side. Tremors of the tongue were noticed; otherwise, the cranial nerves were normal. The left arm was 5 inches (12.7 cm.) shorter than the right, and the bones seemed smaller. The roentgenogram showed that the glenoid cavity on this side was absent, but the head of the humerus was normal in shape and the lower portion ended in a sharp bony process. The muscles were flaccid and flabby, with marked atrophy of the biceps and triceps. Movements of the arm were weak. Movement of the hand was not possible, except slight extension and flexion. The right arm was somewhat weaker than normal, but all movements could be performed. Slight atrophy was present. The biceps jerk was weak on the right and absent on the left; the triceps jerk was absent on both sides. There was marked atrophy and weakness of the muscles of the right lower limb as compared with the left. The knee jerk was present on both sides and was greater on the right. The ankle

15. Fritsch: Ein Fall von Poliomyelitis centralis, Allg. med. Centr.-Ztg. **57**: 137, 1908.

jerk was absent on both sides. The Babinski reflex could not be determined on account of the deformity of the feet. The electrical reactions were as follows:

Right Arm: All muscles responded well to the faradic current.

Left Arm: The deltoid and biceps responded slightly to the faradic current. The triceps did not respond. In all other muscles, there was a diminished response.

Right Leg: The muscles of the thigh and calf responded well to the faradic current. In the peroneal group, the response was diminished.

Left Leg: The quadriceps contracted slightly to the faradic current; the other muscles of the thigh contracted normally. The muscles of the calf did not contract. The peroneal group responded normally. The reaction to the constant current was not tried. The limbs were cold and cyanotic. The viscera were apparently normal.

Course.—The patient was out of the hospital from April until July 12, 1916; when he returned, it was noted that he thought he was growing weaker and that fibrillary twitchings were marked in the muscles of both upper limbs. On March 17, 1917, a note was made that there were tremors of both hands and that these were increased by effort and were more marked on the left side. The fibrillary twitchings were marked. On March 22, 1918, a note was made that the weakness of the right arm had increased and that there was no power in the left arm and hand. The knee jerk on the right side was much increased; on the left side, it was present. The legs were weaker, and braces had to be worn for walking. After June, 1921, the patient used a wheel chair. There was no apparent change in the symptoms until February, 1925, when he became bedfast and complained of difficulty in swallowing; the speech seemed somewhat indistinct and slurring. Atrophy of the tongue was not present. He died of pulmonary edema on March 23, 1925.

Pathologic Studies.—Examination of the brain and spinal cord was made by Dr. Winkelman, who reported the following:

Gross Description: The brain weighed 1,350 Gm. The brain substance was extremely soft, and the pia-arachnoid was thickened and hazy, having the appearance of frosted glass. The basal vessels were large, tortuous and sclerotic. After being hardened in formaldehyde, the brains was cut in a horizontal plane and the following features were brought to view: Marked ventricular dilatation and softening of the inner segments of both lenticular nuclei, more marked on the right. On section of the pons at the level of the entrance of the fifth cranial nerves, numerous small areas of softening could be seen, especially in the basis pontis. The spinal cord was small. When it was cut, gross defects could not be made out.

Microscopic Description: The manifestations can be grouped as follows:

1. The Pia-Arachnoid: The covering of the brain and cord throughout, but especially over the basal structures, such as the pons and medulla, showed a marked fibroblastic proliferation with round-cell infiltration, consisting mainly of lymphocytes, but with occasional plasma cells. Numerous phagocytic elements could also be seen (fig. 1).

2. The Blood Vessels: (*a*) The large blood vessels showed thickening of the walls due mainly to intimal proliferation, but with marked degenerative changes present as shown by fat and calcium deposits. The cells of the adventitia were likewise proliferated and between them was in many instances a considerable amount of round cells, lymphocytes predominating. (*b*) The small vessels for the most part showed thickening of walls and hyalinization. (*c*) In the medium-sized

vessels were two types of changes: (1) thickening of walls with hyalinization; (2) proliferation of the endothelial layer without degenerative manifestations, to such a degree that partial or complete occlusion of lumens was produced. Perivascular collaring with lymphocytes and plasma cells usually completed the picture (Heubner's endarteritis) (fig. 1).

3. The Nerve Tissue: In the region of the basal ganglia as well as in the basis pontis at the level of the fifth cranial nerves were areas of softening with formation of gitter cells and beginning efforts at repair (fig. 2). A great increase in lipoid pigment within the nerve cells as well as around the vessels was found universally throughout the brain.

Fig. 1.—Medium sized vessel, showing intimal thickening with narrowing of the lumen and perivascular infiltration. Meningeal infiltration is seen.

4. The Spinal Cord: The meningeal changes were of the same character as those in the brain and were present to a fairly marked degree. The same type of change in the vessels could also be made out.

The gray matter presented several interesting features. A marked shrinkage and deformity were present in the left anterior horn in the lower cervical region (fig. 3), with decrease in the number of myelinated fibrils. While no such gross deformity occurred in the rest of the spinal cord, with cellular stains it could be easily seen that there was a marked poverty of cells in the anterior horns throughout; this was evident on both sides but apparently was more marked on the left (fig. 4). In the lower cervical region, where the gross deformity occurred, there

were practically no cells on the left side. The cells that were present through the cord showed excess of lipoid (fig. 4).

In the white matter a mild bilateral degeneration of the pyramidal tract could be made out with the myelin sheath stain (fig. 3).

Microscopic Diagnosis: The condition was diagnosed as meningovascular syphilis; arteriosclerosis (senile type) and old poliomyelitis.

COMMENT

Two points are of interest in the study of this case: First, did the patient have poliomyelitis originating in utero? The question can be

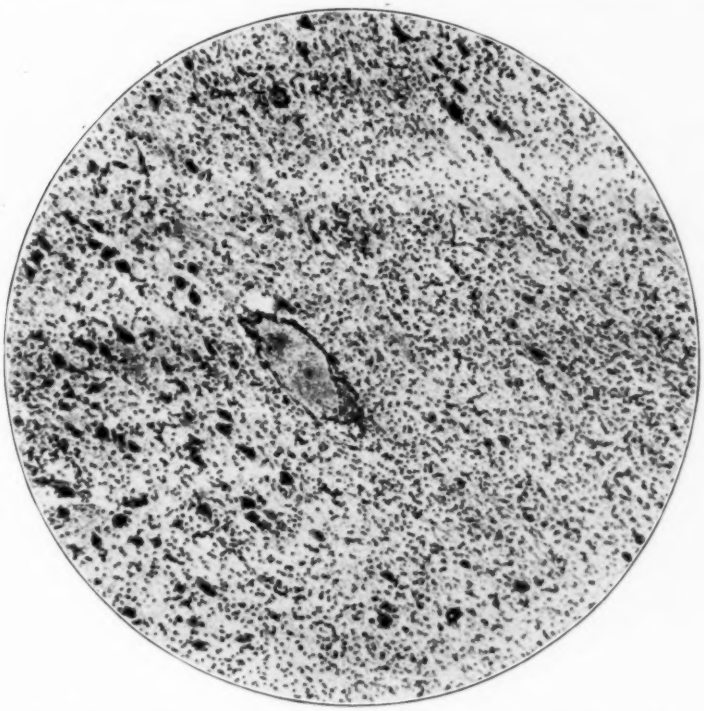

Fig. 2.—Basis pontis, showing area adjacent to a comparatively recent area of softening. Lipoid increase within the ganglion cells can also be made out (Dr. N. Winkelman).

asked, May not the infection have occurred shortly after birth? This is a possibility in this case as well as in some others quoted. It seems clear, however, that the symptoms of the cases reported by both Dejerine and Batten especially were noticed at birth, and it also seems true from the report of Globus [11] that an infection can occur in utero and not cause symptoms until some time after birth. That the symptoms in my case were noticed at that time seems to be well authenticated.

Fig. 3.—Cervical cord, showing shrinkage, and distortion of the left anterior horn with loss of the normal anatomic markings. Mild changes can be made out in both crossed and direct pyramidal tracts (Dr. N. Winkelman).

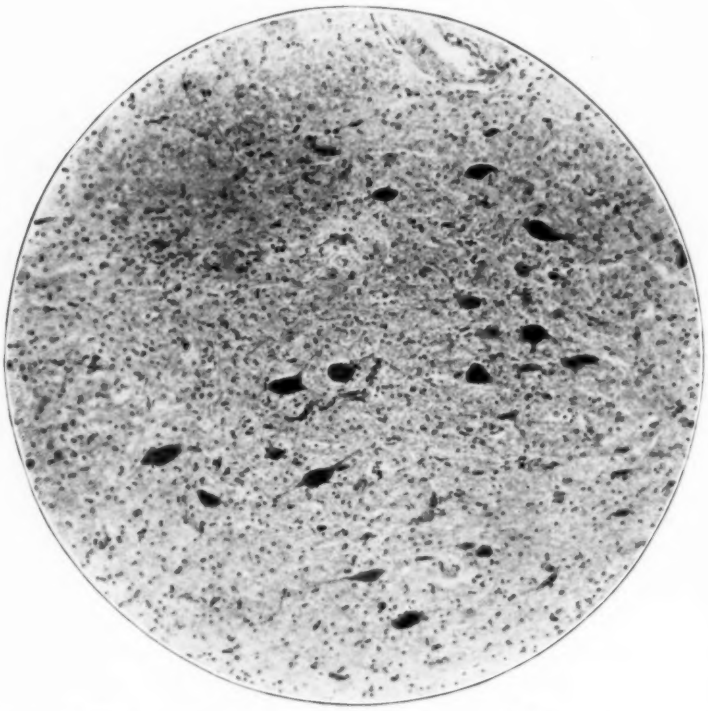

Fig. 4.—Anterior horn cells group from lumbar cord. Decrease in number and pigmentary changes can be made out (Dr. N. Winkelman).

The patient's family, consisting of several brothers, were intelligent and they were positive that the patient had been born with the symptoms described. A cousin, a physician, also stated that in the family this was regarded as true. Study of the cord shows the appearance of old anterior poliomyelitis. In this connection it may be asked, Was the poliomyelitis due to the specific infection which causes this disease or to some other variety, or was it due to syphilis? That the patient had the latter disease is evident, and from his history it seems probable that it was hereditary in origin. That atrophic paralysis of chronic type may be caused by syphilis is well known. No less an authority than Wickman [16] said: "An acute atrophic paralysis may rarely arise from a variety of causes other than the virus which produces Heine-Medin's disease. A few cases are recorded of acute poliomyelitis, probably due to syphilis." If the disease was acquired by the patient in later life, another sort of infection as the cause of the poliomyelitis must be assumed. If the disease was due to the virus of poliomyelitis, how did the patient acquire it? It has been shown that epidemic encephalitis sometimes may infect a fetus if the mother has the disease and also that encephalitis in utero may be acquired from other infections. If so, why not poliomyelitis? It must be remembered that this disease may be present but that the symptoms may be so mild as not to attract attention. It is conceivable, I think, that a mother in this state might transmit the disease. In the cases reported by Globus, Patterson and Carmichael, and Batten, the mothers were not ill. The experiments of Levaditi are important in this connection. That this patient had poliomyelitis, so far as clinical symptoms and pathologic changes are concerned, is evident. That these symptoms were present when he was born seems probable. Whether or not they were due to the specific virus of poliomyelitis or some other form of infection or to hereditary syphilis is doubtful in this case. It seems likely, however, that a true anterior poliomyelitis may occur in utero, although it must be rare.

The second point of interest is the increase in the severity and character of the symptoms after fifty years. In 1903, I reported [17] such a case, reviewed the literature up to that time and collected reports of thirty-seven cases exclusive of mine. Since this, others have been reported. Up to the time the patient entered the hospital, he had been able to walk and supported himself by selling newspapers. From the time of admission he gradually became weaker until he could not

16. Wickman: Acute Poliomyelitis, Monograph, Nervous and Mental Disease Monograph Series no. 16, 1913, p. 13.

17. Potts: A Case of Progressive Muscular Atrophy Occurring in a Man Who Had Had Acute Poliomyelitis Nineteen Years Previously, Univ. Penn. M. Bull. **16**:31 (March) 1903.

walk and fibrillary twitchings of the muscles became noticeable. It is believed that the areas of softening and degeneration of the pyramidal tracts described occurred later in life. This, with later degeneration of the anterior horn cells accounting for the fibrillary twitchings, was the cause of the recrudescence. In this connection, the question whether the fall he had shortly before admission could have been the exciting cause of the exacerbation is worthy of consideration.

AMYOTROPHIC LATERAL SCLEROSIS WITH OBJECTIVE AND SUBJECTIVE (NEURITIC) SENSORY DISTURBANCES

A CLINICAL AND PATHOLOGIC REPORT *

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The diagnosis of amyotrophic lateral sclerosis is usually one of the easiest to make, characterized as the syndrome is by involvement of the anterior horn or nuclear cell groups, that is, lower motor neuron, and the pyramidal tract, or upper motor neuron. Generally, the atrophy begins in the hands and, after a variable period, the degenerative process ascends and involves the bulbar motor nuclei. At some time in the course of the disease, signs of involvement of the pyramidal tract appear. The latter are most evident in the lower extremities, though the hyperreflexia also points to their presence in the region of the atrophies. Most often, involvement of the anterior horn precedes and dominates the picture. Rarely, the pyramidal tract signs appear first and those referable to the lower motor neurons play a secondary rôle. Sensory disturbances, however, either are absent or occur rarely. While subjective disturbances, such as mild pain, occasionally are present, they are usually transient and not of great significance. True neuritic pains are practically unknown in this disease, while objective sensory signs have not been described, so far as we are aware,[1] although pseudopolyneuritic cases with loss of deep reflexes in the lower extremities have been reported.

Generally, the disease is regarded as primarily degenerative, although lead and arteriosclerosis are supposed to play some rôle in the etiology. A definite group of cases has been described in which, presumably,

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1. R. A. Ley, in describing cases of amyotrophic lateral sclerosis of the hemiplegic type, mentions two with "polyneuritic onset." The cases described by Foix, Chavany and Bascourret (Rev. neurol. **1**:822, 1925) as pseudopolynévritique are misnamed, as they presented merely an anterior horn syndrome of the lower extremities and not at all a neuritic syndrome.

syphilis was the causative factor. These have been designated as amyotrophic meningomyelitis.[2] Recently, Wimmer reported a series of cases on the basis of epidemic encephalitis.[3]

We shall report two cases which presented definite neuritic syndromes; the clinical manifestations at first were such as to lead to erroneous diagnoses and, in one case, to fruitless operation. The two cases, in our opinion, are so unusual as to merit detailed report.

REPORT OF CASES

CASE 1.—*A case of proved amyotrophic lateral sclerosis, characterized in the early stages by severe pains (in the lower extremities) of a neuritic or radicular character, atrophy, flaccid paralysis and foot drop, warranting the clinical diagnosis of cauda equina neuritis or tumor. Subsequent disappearance of the neuritic pains and onset of fibrillations, bulbar amyotrophy and pyramidal signs led to the correct diagnosis.*

Clinical History.—S. C., a woman, aged 40, was admitted to the Montefiore Hospital, Dec. 17, 1924, complaining of inability to walk without assistance, of intense pain in the knees and calves when she attempted to stand, greater on the left side, pain in front of the thighs when she stooped and pain in the legs on deep pressure. The family history was unimportant. The menses were regular until the spring of 1923. She then suffered from intense pain in the back before her periods, which occurred every three weeks and lasted twelve days; the flow was profuse and was associated with pain in the back for the first three days. An operation was performed on the gallbladder in 1919. Since June, 1924, nocturia had been present (urination occurring from five to six times during a night). The present illness began in July, 1923, with cramplike pain in the legs, which became progressively worse. The lower extremities grew weak. In June, 1924, she entered another institution where she remained ten weeks. There, the condition was regarded as multiple neuritis. Although some improvement occurred, the severe pain and weakness gradually returned. She lost 20 pounds (9 Kg.), and on admission to the hospital weighed 98 pounds (44.5 Kg.).

Neurologic Examination.—The patient could sit up, but could not stand or walk unsupported. Attempts at moving the lower extremities elicited an expression of anxiety and pain. The fundi showed staphyloma incidental to high myopia. The pupils were irregular; they reacted normally to light and in accommodation. The cranial nerves were otherwise normal.

The upper extremities had normal tone and power. The lower extremities showed distinct atrophy from the thighs to the toes, greater in the feet and on the left side. There was marked weakness of the muscles of the legs with bilateral foot drop; this was also greater on the left. She had a steppage gait. There was marked limitation of voluntary power throughout the lower extremities, greater on the left. Fibrillations were not present. The skin of the feet was dry and atrophic, and there was venous stasis. The knee joints were apparently swollen, although there was not any limitation to passive movement.

In the upper extremities, the deep tendon reflexes were increased; the Hoffman sign was not present. The reflex in the lower part of the left side of the abdomen

2. Martin, J. P.: Amyotrophic Meningo-Myelitis, Brain **48**:153 (June) 1925.

3. Wimmer, A.: Chronic Epidemic Encephalitis, London, William Heineman, 1924.

was the only one elicited. Both knee jerks and the right ankle jerk were diminished; the left ankle jerk was absent. The Babinski and Rossolimo toe signs were not elicited. An exhaustible clonus of the right ankle was present.

Pain, touch, position, joint and vibratory sensation were normal throughout, with the possible exception of an area of hypalgesia on the external surface of the left ankle. The soles were extremely sensitive to scratching. There was tenderness in both calves and thighs on pressure. She complained of cramplike pains in the lower extremities. Ataxia and incoordination were not present. Spinal tenderness and rectal, vesical and trophic disturbances were not observed.

The case was considered one of peripheral neuritis or an infectious radiculitis.

Course.—On Dec. 12, 1924, an examination showed tactile sensibility diminished over the left second sacral dermatome, a belt of hyperesthesia corresponding to

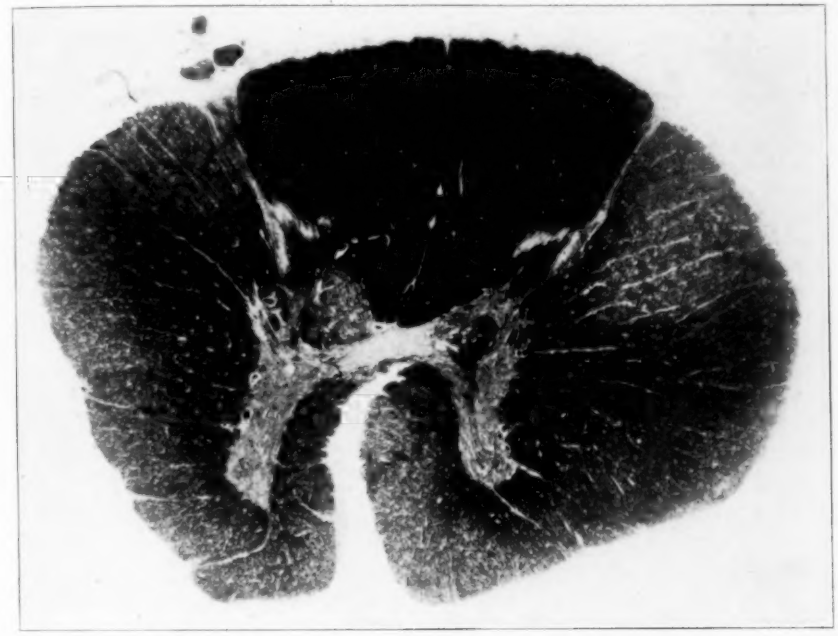

Fig. 1 (case 2).—Transverse section through upper dorsal segment. Myelin sheath stain. Showing demyelinization most pronounced in indirect pyramidal tract and anterior column of one side.

the first and second lumbar segments, and wasting of the muscles of both lower extremities, especially on the left, with greater involvement of the anterior than of the posterior groups. The toes were in plantar flexion but could be extended fairly well. A right Babinski sign, ankle clonus and the Rossolimo sign were now elicited. The right knee jerk was diminished and the left absent. The right ankle jerk was lively and the left absent. Trophic disturbances were noted in the toe nails and the skin of the feet. It was concluded that the presence of the lively ankle jerk on the right side, of pathologic toe reflexes and of asymmetry pointed to a tumor of the lower cord, involving also the cauda equina. A progressive inflammatory process was also considered.

On Feb. 23, 1925, it was noted that the right ankle jerk was elicited, with clonus. The Rossolimo and Babinski signs were absent. The patient had spontaneous cramplike pains. The symptoms spoke against neuritis and pointed to involvement of the cord. In view of the uncertainty, exploration was decided on to determine the presence or absence of a tumor.

On March 2, an inflammatory condition involving the peripheral nerves, roots and cord in the lumbosacral region was seriously considered. At the same time,

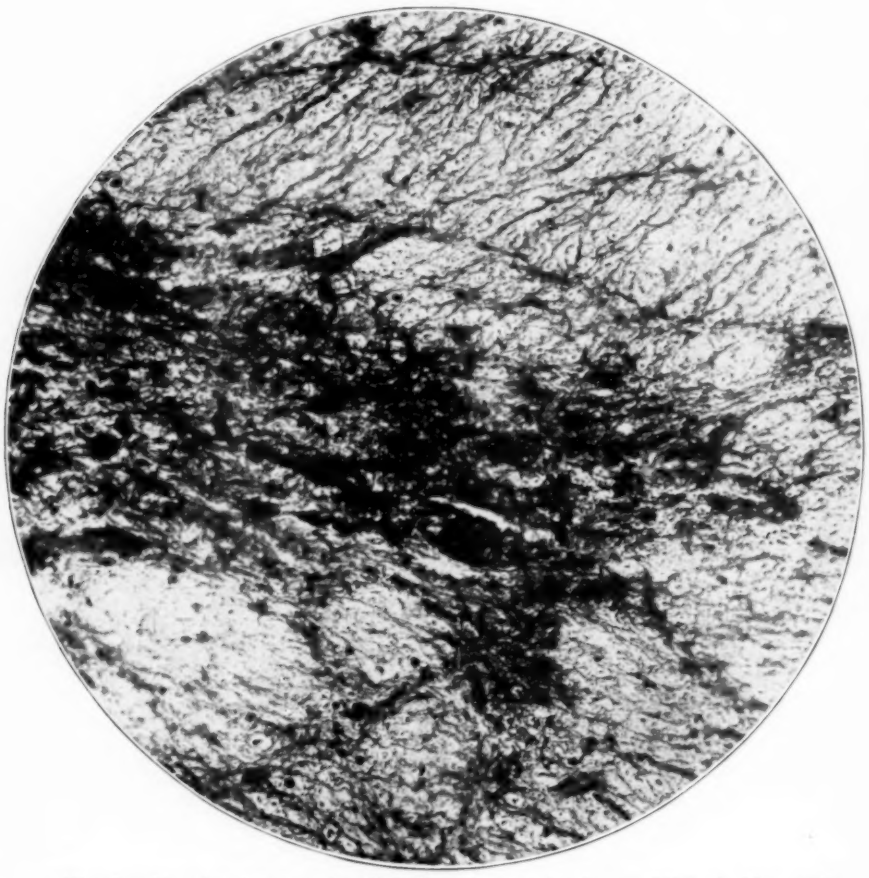

Fig. 2.—Showing increase in glial fibers in anterior horn. Victoria blue stain.

great loss of voluntary power in the lower extremities, with wasting, marked diminution of the deep reflexes, definite hypesthesia and hypalgesia in the region of the left dermatome also led another observer to the diagnosis of neoplasm of the cauda equina.

On March 7, a laminectomy was performed. The spines and laminae of the eleventh and twelfth dorsal and the first and second lumbar segments were removed. The lower cord and cauda equina were carefully examined but nothing pathologic was found.

On July 7, the jaw reflex was found to be increased. On October 6, the condition of the legs grew definitely worse. In addition to the absent reflexes, there was diminution of sensation in both feet, which were very cold. The upper extremities showed lively reflexes. All forms of sensation were perceived in the left upper extremity, but the patient stated that she did not feel pain, touch and temperature as well as on the right side, in the distribution of the fifth cervical to the first dorsal segment inclusive. The left pupil was smaller than the right;

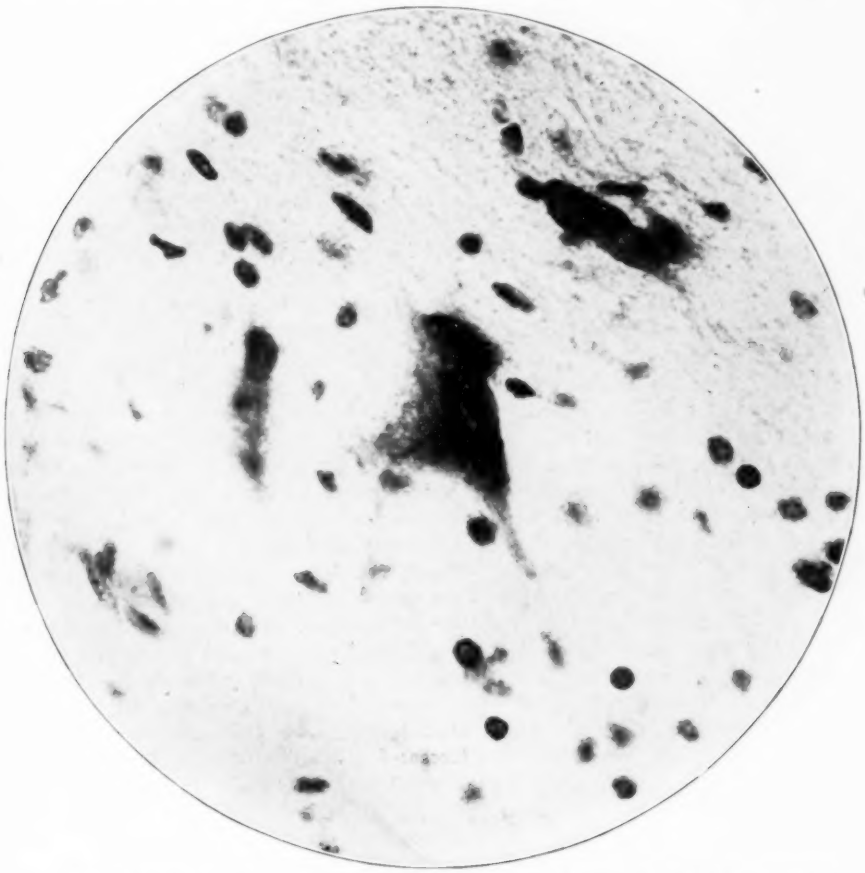

Fig. 3 (case 1).—Ganglion cell from nucleus ambiguus, showing chromolysis and eccentric position of nucleus. Cresyl-violet stain. Zeiss 4 mm. ap.

the jaw jerk was lively, and there was marked tenderness of the seventh and eighth cervical spines. Then the presence of a lively jaw jerk, the lively reflexes in the upper extremities and the Hoffman sign were suggestive of amyotrophic lateral sclerosis. The severe neuritic pains which caused spastic contraction for several months gradually began to wane.

On Nov. 23, 1926, complete flaccid paralysis of both lower extremities, with loss of deep reflexes and bilateral foot drop, were noted. The plantar response and the Babinski toe sign were not obtained. The upper deep reflexes were still

lively. There was atrophy of the thenar and hypothenar eminences and of the interossei. Fibrillations in the right triceps and deltoid and marked fibrillations of the tongue were present. There was no paralysis of the palate, but the speech was slightly palatal. Both temporal muscles showed atrophy. The abdominal reflexes were absent. At this time, all forms of sensation were intact everywhere.

The atrophies in the upper extremities and the tongue reflected marked disease of the anterior horn and nuclear disease, while the hyperreflexia pointed to involvement of the pyramidal tract—a syndrome of amyotrophic lateral sclerosis. The history of severe pain in the legs, and the completely progressive flaccid paraplegia, with the transient presence of clonus, certainly did not fit in with the usual picture of amyotrophic lateral sclerosis. The question was whether we were dealing with two entities or with an unusual combination of an inflammatory and degenerative process, the former affecting the lower extremities and the latter the upper.

Laboratory Data: The blood pressure was 120 systolic and 80 diastolic. The serology of the blood and spinal fluid was normal. Spinal and manometric studies gave normal results. The blood count was normal. Examinations of the urine repeatedly gave normal results. General medical examination also gave negative results.

On Dec. 23, 1926, atrophy and fibrillations of the tongue were marked. The deep reflexes of the upper extremities were exaggerated, more on the right. The jaw reflex was hyperactive. The abdominal reflexes, ankle jerks and knee jerks were absent. The Babinski toe sign was not present. The flaccid paralysis of the legs with a bilateral foot drop remained as before. Sensory examination did not reveal any abnormalities. Coordination was normal in the upper extremities.

In August, 1927, the progress of the disease was evident. There was marked atrophy of the tongue and of the facial and temporal muscles. Fibrillations were seen in the tongue and in the facial, pectoral, neck, biceps, triceps, serrati, levatores scapulae and thigh muscles. The jaw and pectoral reflexes were active. Speech was dysarthric and nasal (bulbar). Disturbances in the bladder were not noted. The patient had dysphagia. Again there was not any sensory involvement.

On Jan. 24, 1928, clonus of the jaw was observed. The small muscles of the hand and the sternocleidomastoid, temporal, buccinator, masseter and lingual muscles were atrophic. Dysarthria was marked. She did not regurgitate food and could masticate fairly well. Dysphagia was present, however. She could not lift her head from the pillow. The pupils reacted but did not hold well to light; the right reacted better than the left. Except for the jaw jerk, all reflexes were absent. Psychic disturbances were not noted.

The bulbar paralysis progressed, and on March 3, 1928, the patient died suddenly of respiratory paralysis.

Neuropathologic Report.—Macroscopic examination of the brain showed a moderate degree of arteriosclerosis. The meninges were normal. Gross abnormalities were not noted on vertical section. The spinal cord did not show any gross abnormalities.

In total vertical sections of the brain stained for myelin sheaths, there was slight paling out of the corona radiata on both sides, but this did not surpass the picture which one is accustomed to observe in corresponding sections of other chronic diseases of the central nervous system. Under high power magnification, demyelinization could not be made out; the same was true of the internal capsules. In transverse sections through the pons and medulla oblongata, demyelinization of the pyramidal tracts could not be made out. With cresyl violet stain, the

central region did not show any abnormalities in cytoarchitecture. The same may be said for the basal ganglia which were examined.

Pathologic changes were not observed in the trigeminal nuclei. The same was true of the reticular nuclei. Different stages of degeneration from slight swelling to complete destruction, were present in the facial nucleus. A similar picture was seen in the nucleus ambiguus and the motor nuclei of the accessory and hypoglossal nerves. The blood vessels and meninges of the brain did not show any marked pathologic changes.

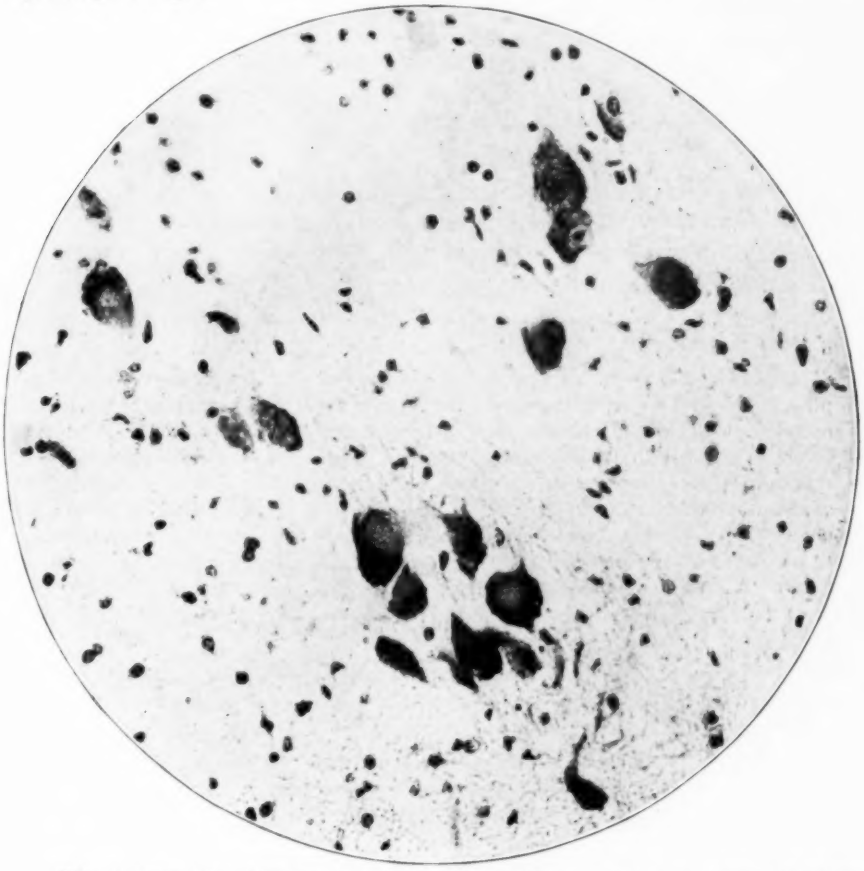

Fig. 4 (case 2).—Nucleus facialis, showing different stages of chromatolysis and swelling of ganglion cells. Cresyl-violet stain. Zeiss 8 mm. ap.

In transverse sections stained for myelin sheaths, there was throughout the whole spinal cord, distinct paling of the lateral columns extending beyond the area of the crossed pyramidal tracts. The anterior and posterior columns were normal. In Bielschowsky stains of longitudinal sections, the axis cylinders were swollen and distorted in the same area. Glia stains revealed slight increase of glial fibers in both longitudinal and transverse directions. In Nissl stained sections both anterior horns showed marked increase of glia nuclei. The anterior horn cells were diminished in number, most strikingly in the anterior and lateral groups of

the cervical region. The remaining ganglion cells showed atrophy. In the lower lumbar segment, there was an acute hemorrhage in both anterior horns imposed on an old glia scar. Most of the anterior horn cells of this region had disappeared, but those left showed severe degeneration. The sacral segment showed relatively less involvement than the higher segments. Definite pathologic change could not be made out in sections through the cauda equina. The myelin sheath of the nerve fibers were well preserved throughout, and there were no remains of any inflammatory reaction. Definite neuronophagia could not be made out. The blood vessels of the spinal cord did not show any marked changes, and there were no meningeal reactions.

Comment.—The combined disease of the lateral columns with anterior horn cell degeneration presented the typical picture of amyotrophic lateral sclerosis. There is no basis for the assumption that vascular or infectious disease played a rôle in the production of the histologic picture. One has to assume, therefore, a purely degenerative condition.

CASE 2.—*A case of proved amyotrophic lateral sclerosis, beginning with signs of peripheral neuritis in the lower extremities and, after a considerable interval, developing typical evidence of amyotrophic lateral sclerosis in the upper extremities and medulla.*

Clinical History.—L. H., a man, aged 48, was admitted to the Montefiore Hospital, April 1, 1926, complaining of inability to walk and coldness in the lower extremities. The family and past histories were without significance. The present illness began, late in 1924 (eighteen months prior to admission), when he noticed marked weakness in the right foot and leg. The disability spread to the left leg so that he could walk only with a cane. The feet were not stiff, but he was unable to lift them and had to use crutches. There were no symptoms referable to the upper extremities. Three months before admission, he noticed that cold air caused the lower extremities to sting. History of paresthesias or sphincteric disturbances was not elicited. The voice had not changed. Difficulties in chewing, swallowing, breathing or talking were not noted.

Physical Examination.—Except for the presence of a moderate arteriosclerosis, with a blood pressure reading of 160 systolic and 105 diastolic, the general physical examination gave negative results.

Neurologic Examination.—Early in April, 1926, neurologic examination revealed the following: The fundi showed moderate arteriosclerosis. The left pupil was irregular, the right being larger than the left; both reacted sluggishly to light and better on accommodation. The left eye converged poorly; other extraocular movements were normal. Except for an increased jaw reflex, greater on the left, and a fine tremor of the tongue, the cranial nerve functions were normal.

The upper extremities were normal. He walked with a flaccid, steppage gait, and had bilateral foot drop. There was limited power of flexion at the knee and ankle joints. He could not walk without crutches. While there was only limited power in the flexor group, the weakness in the extensors was marked. Flexion and extension were markedly impaired at the hip joints, with greater involvement on the right side. Fibrillations of the muscles of both thighs and legs were marked. There was generalized atrophy of the thighs and legs on both sides, more marked on the right. Coordination was slightly impaired in the upper extremities; it could not be tested in the lower extremities.

The patient was uncooperative; however, there appeared to be some hyperesthesia and hyperalgesia bilaterally in the distribution of the first lumbar dermatome and hypesthesia and hypalgesia in the third, fourth and fifth lumbar segments. There was impairment of vibratory sensation below the knees. Joint, muscle and tendon sense was normal in grosser tests, but seemed impaired in the testing of finer degrees of movement. Examination of the temperature sense was totally unreliable. Perianal anesthesia was not observed. Tenderness of the calves was present on deep pressure. The mental status was essentially normal.

The presence, at one time, of a definite stocking, and a less evident glove, type of diminished sensibility led to the diagnosis of multiple neuritis; on the other hand, the atrophy with the fibrillary twitchings pointed to an atypical chronic progressive muscular atrophy.

Course.—On April 25, 1926, the electrical reactions showed marked diminution to faradic stimulation in the legs. Cathodal closure contraction equaled anodal closure contraction; it required a greater strength of current than normal. The hamstrings revealed a vermicular response (partial reaction of degeneration). The muscles of the upper extremities responded normally.

On July 2, an apparent atrophy of the right thenar and hypothenar eminences was first noted. By August 19, 1927, a marked progression of the atrophies was

Tests for Reflexes

Reflexes	Right	Left
Biceps	+++	++
Triceps	+++	++
Radials	+++	0
Knee-jerks	+	+
Ankle-jerks	+	+
Babinski sign and clonus	0	0
Abdominal—upper	++	+
lower	+	+
Cremasteric	Absent	Absent

evident. All the musculature of both shoulder girdles was affected. Fibrillations were likewise more widespread. There was much less power in the lower extremities. The pectoral and latissimi muscles seemed intact. The patient was unreliable; nevertheless, there seemed to be definite hyperalgesia in the lower sacral dermatomes. There was beginning atrophy with fibrillations of the tongue. Difficulty was not experienced in swallowing; the sphincters were intact.

On August 30, the atrophies and fibrillations were present in the small muscles of both hands, forearms and arms. There were not any pathologic reflexes, and all the deep tendon reflexes were absent, except the left biceps and triceps jerks, which were markedly diminished. The abdominal and cremasteric reflexes were absent. The feet and legs were edematous and cold. The condition in the lower extremities was regarded as practically the same as on admission. The sensory disturbances were just as vague but, nevertheless, present. The addition of the muscular atrophy of the trunk, neck and shoulder girdle muscles, the typical involvement of the intrinsic hand muscles, the fibrillations in all the atrophied muscles and tongue, and a hyperactive jaw reflex pointed to an atypical form of amyotrophic lateral sclerosis. This was atypical because: (1) it apparently began in the peripheral nerves of the lower extremities; (2) there was slight involvement of the pyramidal tracts; (3) there was a long interval of apparent arrest of the disease from the time of the involvement of the lower extremities to the time of involvement of the upper extremities, and (4) there were early sensory disturbances involving fine touch and pain in the distribution of peripheral nerves.

On Oct. 3, definite fibrillations of the tongue were present. The breathing was rather labored. The patient was practically helpless. He could raise the head slightly, but could not support it well in the sitting position. He died in November, 1927, of bronchopneumonia.

Laboratory Data.—On April 7, 1926, the spinal fluid was clear, and showed ten cells, a faint trace of sugar and an absence of globulin. The Wassermann test was negative. The gum mastic curve was 2221111000. The manometric examination did not reveal any block. Examinations of the urine gave negative results. Roentgen-ray examination of the lumbar spine showed moderate arthritic changes of the hypertrophic type, especially marked in the fourth lumbar vertebra. Gross changes had not occurred in the region of the sacrum and coccyx.

Neuropathologic Report.—Macroscopic examination of the brain showed that the vessels and meninges were normal. The brain was cut vertically. Gross abnormalities were not noted. The meninges of the spinal cord were normal. At the eighth cervical and first dorsal level there was thinning alternating with bulging of the spinal cord. The rest of the spinal cord looked apparently normal. The cervical cord, cut at the fifth cervical level, showed a marked yellowish appearance of the gray matter. The anterior horns seemed to be atrophic while there was no general atrophy of the cord itself. At the first dorsal level, there was destruction of the gray matter on the left side which was replaced by a cavity partly filled out with coagulated masses which could easily be removed.

At the second dorsal segment, the cavity disappeared, but gross atrophy of the gray matter was still seen, most pronounced in the right anterior horn. At the sixth dorsal level, the cord showed atrophy of both anterior horns. At the second lumbar level the gray matter had a yellowish appearance and seemed to be atrophic, more on the left than on the right.

The nerve fibers of the spinal cord were stained with Sudan III, Loyez, Rio-Hortega IV, Bielschowsky and Nissl stains. There was an accumulation of fat droplets enclosed in round cells in the region of the right lateral pyramidal tract and throughout the whole of the right anterior column. This region showed darker staining with hematoxylin, as compared with the rest of the white matter of the spinal cord. Glia stains revealed an increase in fibrous glia at this region. The myelin sheaths were markedly swollen, but had not yet completely disappeared. The process of beginning demyelinization of the right lateral pyramidal tract and the right anterior column could be followed throughout the whole spinal cord and even extended into the lower lumbar segments. The left half of the spinal cord and the posterior columns were spared from this degenerative process. In Loyez' stain, the right anterior horn throughout the whole cervical cord seemed to be reduced in size as compared with the left. This reduction also included the posterior horn and was striking in Clarke's column throughout the dorsal segments. Nissl stain showed intense increase of glia nuclei throughout all the gray matter on the right side and was also marked in the anterior half of the left anterior horn. The anterior horn cells seemed to be diminished in number in both horns. Under higher magnification, the remaining cells were seen to be reduced in size; they were round and globular, the Nissl substance had disappeared and the cytoplasm was replaced by fine granular masses. The same process of swelling and degeneration was also marked in Clarke's column, while the lateral horn cells were fairly well preserved. In the lower dorsal region there was dense, small-celled infiltration of the pia-arachnoid, which in itself did not yet show any connective tissue reaction (acute leptomeningitis). The anterior horn cells in the lower lumbar and sacral regions were fairly well preserved. Sections through the cauda equina did not reveal any marked pathologic changes.

The process of myelin sheath degeneration did not extend into the pyramidal tract. Stained with cresyl violet, degeneration of varied degree was seen in most of the motor nuclei. The nucleus ambiguus and nucleus facialis were mostly involved, and the nuclei of the glossopharyngeal and accessory nerves to a less degree. The nucleus motorius nervus trigemini was only slightly involved, as well as the reticular nuclei of the pons. In transverse sections through the whole brain, the internal capsule did not show demyelinization. There were not any significant vascular or meningeal changes. The examination of sections throughout the central area stained with cresyl violet did not show any marked pathologic changes of the different ganglion cells.

Comment.—The essential features of this case were the changes in the spinal cord, which were more pronounced in the lateral and anterior columns on the right side than on the left, while the anterior horn cells were more evenly affected on both sides. This unilateral preponderance distinguished the case from the classic picture of amyotrophic lateral sclerosis. The absence of vascular and meningeal changes favored the diagnosis of a purely degenerative process.

SUMMARY AND CONCLUSION

The two cases described were so unusual that for a long time the diagnosis of amyotrophic lateral sclerosis was not even suspected. Both began with signs and symptoms in the lower extremities, in itself an unusual feature, and were characterized by sensory disturbances of a neuritic nature. In case 1, the pains were so severe in the lower sacral dermatomes that a diagnosis of tumor of the cauda equina or neuritis was made. In view of this fact, a laminectomy was performed but a pathologic process was not found. After many months, the pains gradually subsided, and the objective sensory changes disappeared. It was only with the advent of segmental atrophies, fibrillations and hyperreflexia higher up that the true condition, subsequently confirmed by pathologic study, became apparent. In case 2, although the pains were much less marked, the objective sensory disturbances and the nerve tenderness were so definite that for a long time the diagnosis of multiple neuritis was entertained. Here, too, the signs and symptoms began in the lower extremities, and it was only with the subsequent appearance of nuclear and lateral column signs higher up that the correct diagnosis was made.

The question of the pains in this syndrome has perplexed us a great deal, but we are unable to explain either the objective or the subjective sensory manifestations. Despite the fact that extensive pathologic investigations were made, involvement of the nerves, roots or cauda equina was not found; and, while the early clinical course pointed to an inflammatory process, the pathologic changes subsequently revealed were degenerative. We are aware of the existence of so-called central pains,

particularly in syringomyelia and central gliosis, and the assumption that changes in the zone of Lissauer or even in the posterior horns may give rise to pains. It is possible that the degeneration found in those regions in our cases may have been the cause of the pains, but that will not account for the type and neuritic distribution of the pain and the objective sensory changes. In view of the long duration of the syndromes, an inflammatory process of some kind might still be assumed to have been present at the very onset, but the utter absence of such signs on microscopic study speaks against such an assumption. We must, therefore, be content with the simple record of two cases of amyotrophic lateral sclerosis, with the onset of objective and subjective sensory disturbances.

TABES DORSALIS

PATHOLOGY AND PATHOGENESIS; A PRELIMINARY REPORT *

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Of the numerous theories of the pathogenesis of tabes dorsalis, only two deserve consideration. According to one theory, advocated by Strümpell,[1] Spielmeyer,[2] Hauptmann [3] and others, tabes is an endogenous disease process. It is supposed to be caused by a syphilitic toxin which "selectively" affects certain parts of the posterior columns and causes their degeneration. The other, equally popular, theory is that tabes is an exogenous disease, which originates outside the spinal cord, either at the so-called area of Obersteiner-Redlich or in the "radicular nerve" of Nageotte.

Obersteiner and Redlich [4] called attention to the fact that at the place of their passage through the pia, the posterior roots "seem to be deprived" of some of their myelin, and, as a result of this, exhibit there a visible constriction; as the axons in this area lie unprotected and naked, they become the "locus minoris resistentiae," that is, particularly vulnerable; any pressure on them, whether caused by a thickened and infiltrated pia, by a sclerosed blood vessel or by other factors, may produce degeneration of the intraspinal prolongations in the posterior columns. Practically similar views were advocated by B. Sachs.[5] He stated that it would be proper to define tabes as

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1. Strümpell, A.: A Text-Book of Medicine, third American edition, London, H. K. Lewis, 1901, p. 961.

2. Spielmeyer, W.: Die Trypanosomenkrankheit und ihre Beziehungen zu den syphilogenen Nervenkrankheiten, Jena, Gustav Fischer, 1908; Experimentelle Tabes bei Hunden (Trypanosomentabes), München. med. Wchnschr. **53**:2338, 1906; Zur Pathogenese der Tabes, Ztschr. f. d. ges. Neurol. u. Psychiat. **84**:257, 1923; **91**: 627, 1924 and **97**:287, 1925.

3. Hauptmann, A.: Der "Weg über den Liquor," Klin. Wchnschr. **4**:1297 (July 2) 1925.

4. Obersteiner, H., and Redlich, E.: Ueber das Wesen und Pathogenese der tabischen Hinterstrangs-degeneration, Obersteiner's Arb. **2**:158, 1894, and **3**:192, 1895.

5. Sachs, B.: Syphilis and Tabes Dorsalis, New York M. J. **59**:1 (Jan.) 1894.

a degeneration of the posterior root fibers as they enter the gray and white matter of the spinal cord. He also hinted that affection of the posterior roots by syphilitic meningitis is responsible for the changes seen in tabes.

Nageotte [6] placed the starting point of the lesion of the posterior root, not in the constriction area of Obersteiner-Redlich, but in that portion of the posterior root which lies between the spinal ganglion and the subarachnoid space, or rather the arachnoid membrane where, as André-Thomas and Hauser [7] expressed it, it "deflects" to the posterior root (fig. 1). Here the anterior and posterior roots meet to form what Nageotte called the "radicular nerve." In tabes, according to Nageotte, this nerve is the seat of a syphilitic inflammation with an accumulation of hematogenous elements (lymphocytes and plasma cells) and of so-called "embryonal cells." The cell accumulation by its pressure or in some other way (irritation) affects the roots and causes their degeneration.

Nageotte's teaching was somewhat modified by Richter.[8] According to this investigator the area of Nageotte shows practically no hematogenous cells in cases of so-called pure tabes; that is, in those which are not complicated by paresis or by syphilis of the cord. Instead, it is infiltrated almost exclusively with what he called "granulation" cells or syphilitic granulomas—a local reaction of the root nerve to the presence of spirochetes. In cases of long standing, the root nerve is invaded by fibroblasts; it is these which are mainly instrumental in the causation of the degeneration of the posterior roots. Richter also assumed that the cerebrospinal fluid in which the posterior roots are bathed is full of spirochetes, and that this "spirochetosis" of the fluid affects the posterior roots and causes their degeneration. André-Thomas and Hauser,[7] Heym,[9] Alford,[10] Haupt-

6. Nageotte, I.: La lésion primitive du tabes, Bull. Soc. anat. de Paris **69**: 808, 1894; Compt. rend. Soc. de biol. **52**:354, 1900, and **54**:1080 and 1226, 1902; Rev. neurol. **11**:1, 1903; Pathogénie du tabes dorsal, Paris, G. Naud, 1903.

7. André-Thomas and Hauser, G.: Étude sur les lésions radiculaires et ganglionnaires du tabes, Nouv. iconog. de la Salpêtrière **15**:290 and 412, 1902.

8. Richter, Hugo: Zur Histogenese der Tabes, Ztschr. f. d. ges. Neurol. u. Psychiat. **67**:1, 1921; and Neurol. Centralbl. **33**:882 (July 16) 1914 (preliminary report); Sur la pathogénie du tabes, Schweiz. Arch. f. Neurol. u. Psychiat. **9**:65, 1921; Bemerkungen zur Histogenese der Tabes, Arch. f. Psychiat. **67**:295, 1923; **70**:529, 1924, and **72**:318, 1924.

9. Heym, A.: Wie entstehen die pathologisch anatomischen Veränderungen bei Tabes dorsalis? Neurol. Centralbl. **28**:1255, 1909.

10. Alford, L. B.: Studies on the Pathogenesis of Tabes Dorsalis, Tr. Am. Neurol. A. **48**:256, 1922.

mann,[3] Spitzer,[11] Sven Ingvar [12] and others also shared the view that the "toxicity" of the cerebrospinal fluid is an important factor in the production of tabetic changes in the cord.

It must be conceded that the foregoing theories explain only some of the phenomena pertaining to the pathology and pathogenesis of tabes dorsalis. Other important features remain unexplained. For instance, the endogenous or toxic theory fails to account for the degeneration of the posterior roots and for the preponderant degeneration of the

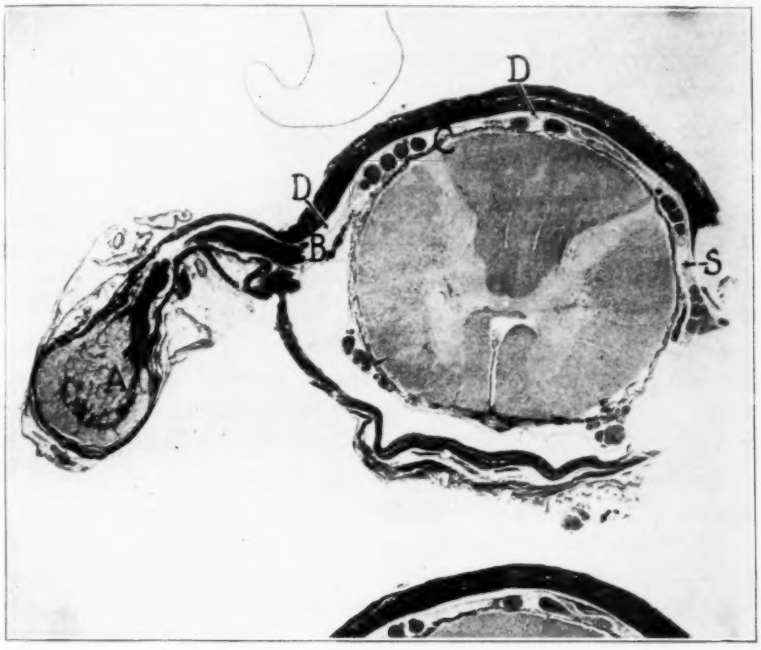

Fig. 1.—A nontabetic cord (upper thoracic region). The broad dark band is the dura; it is more developed around the posterior columns and extends over the spinal ganglion (*A*) where bundles of the posterior root fibers originate. At *B* the root enters the subarachnoid space (also marked *S*); the portion between *B* and the ganglion *A* is the area of Nageotte occupied by what he terms the radicular nerve. From *B* to *C* is the arachnoid portion of the posterior root of which, especially on the right, the intramedullary entrance zone can be seen as well as the columns of Burdach and Goll; at *D.D.*, the subdural space is represented by a narrow space extending over the radicular nerve and even the spinal ganglion. Over the anterolateral columns, the subdural space is broader in this picture. Weigert-Kulschitzky stain.

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11. Spitzer, H.: Zur Pathogenese der Tabes Dorsalis, Obersteiner's Arb. **28**: 227, 1926.

12. Sven Ingvar: Zur Morphogenese der Tabes, Acta med. Scandinav. **65**: 645, 1927.

posterior columns, especially of that portion which represents the posterior roots; the exogenous or mechanical theory does not explain the discrepancy in the degree of degeneration of the intraspinal as compared with that of the extraspinal segments of the posterior roots (Richter). In addition, Bielschowsky [13] and Schaffer [14] pointed out that even with the finer histologic methods it is not possible to demonstrate an exact or definite point from which the degeneration of the posterior roots starts.

On the other hand, André-Thomas and Hauser,[15] Spielmeyer [16] and others called attention to the lack of correspondence between the extent of the mesodermal and the parenchymatous changes. The former, for instance, may be intense while the latter, in contrast, may be mild, and vice versa; both, as is the case in paresis, are independent phenomena. That the intensity of the mesodermal changes does not reflect on that of the parenchyma was emphasized also by Steiner.[17] In syphilitic lesions of the peripheral nerves, he found lack of nerve degeneration in the presence of hyperplasia of the perineurium and endoneurium.

Since many other features cannot be explained by either of the two dominant theories alone, Schaffer, Bielschowsky and Jakob [18] were inclined to a "mixed" view: that though one deals in tabes with a primary degeneration of the posterior columns, a great deal of inflammation also takes place in the areas of Obersteiner-Redlich and Nageotte.

My studies of tabes cover a period of practically twenty-five years. Begun in 1903, they had to be discontinued because of the lack in Chicago, at that time, of suitable laboratory facilities for experimental and pathologic studies, especially of as difficult and complicated a problem as tabes dorsalis. For this reason, my studies were confined to gross anatomic changes and theoretical considerations.[19] Renewed

13. Bielschowsky, M.: Ueber den Bau der Spinalganglien unter normalen und pathologischen Verhältnissen, J. f. Psychol. u. Neurol. **11**:188, 1908.

14. Schaffer, Karl: Tabes Dorsalis, in Lewandowsky, Handbuch der Neurologie **2**:1022, 1911.

15. André-Thomas and Hauser, G.: Note sur les lésions radiculaires et ganglionnaires du tabes, Compt. rend. Soc. de biol. **54**:979, 1902.

16. Spielmeyer, W.: Zur Frage vom Wesen der paralytischen Hirnerkrankungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **1**:105, 1910.

17. Steiner, G.: Beiträge zur pathologischen Anatomie der peripheren Nerven bei den metasyphilitischen Erkrankungen, Arch. f. Psychiat. **49**:667, 1912.

18. Jakob, A.: Die Entzündungsfrage im Zentralnervensystem, Jahresk. f. ärztl. Fortbild. **10**:1 (May) 1919.

19. Hassin, G. B.: Pathogenesis of Locomotor Ataxia, Clin. Rev. **18**:258, 330, 413, 1903; Contribution to Obersteiner-Redlich's Theory of Tabes Dorsalis, M. Rec. **65**:168, 1904.

in 1914, in Prof. A. Jakob's laboratory (Hamburg), they again had to be discontinued because of the outbreak of the World War. However, they advanced sufficiently to justify a preliminary report.[20] Professor Jakob was kind enough to continue the study of the material I left in Hamburg, including some cases of his own;[21] after the termination of the war he sent me, through a representative of a German commercial firm, my slides, photomicrographs, blocks of tissues and also a valuable collection of anatomic slides. The parcels, however, never reached me. I had to begin my studies all over and have continued them, with frequent interruptions, to the present day. They are not finished by any means but as they reveal, in my opinion, some new facts and offer new suggestions as to the pathogenesis of tabes, I considered them of sufficient interest to be recorded in the form of another preliminary report. The results may be summed up thus: In tabes dorsalis, degenerative changes in the spinal cord and certain portions of the posterior roots are combined with inflammatory phenomena in all the three meninges and their spaces (epidural, subdural and subarachnoid). One result of this inflammation is an obstruction of the perineural root spaces; consequently, there is an interference with the escape of spinal fluid; this causes stagnation of tissue fluids in the posterior columns of the spinal cord and results in their ultimate degeneration.

MATERIAL STUDIED AND METHODS EMPLOYED

My material, exclusive of the cases studied at Hamburg, comprised eighteen cases of pure, uncomplicated tabes, eight cases of spinal syphilis and thirteen cases of mixed nature (carcinoma, pachymeningitis, tumors and normal cords). The roots were removed together with the spinal ganglia and were sectioned either longitudinally or transversely. Whenever it was possible, for instance in the cervical region, sections were made through the spinal ganglia, the roots and the meninges, including the dura. In the first years of my studies I paid attention mainly to the condition of Nageotte's radicular nerve and of the pia-arachnoid. Subsequent studies also included the dura and the epidural tissues. Paraffin, celloidin and, when possible, frozen sections were used. Of the staining methods, those of hematoxylin with eosin and van Gieson were found sufficient, especially for the study of the meningeal and other cellular changes, while the spinal cord was studied with the methods of Bielschowsky and Alzheimer-Mann or with these

20. Hassin, G. B.: Beiträge zur Histopathologie der Tabes dorsalis, Neurol. Centralbl. **33**:1138, 1914; Histopathological Studies in Tabes Dorsalis, J. Nerv. & Ment. Dis. **42**:699, 1915.

21. Jakob, A.: Einige Bermerkungen zur Histopathologie der Paralyse und Tabes, mit besonderer Berücksichtigung der Spirochätenbefunde, Arch. f. Psychiat. **65**:191, 1922.

two methods combined. In every case the method of Weigert-Pal, sometimes counterstained with that of van Gieson, was used; a number of specimens were studied also for the presence of spirochetes, some with the methods of Levaditi or Noguchi, and some with those of Jahnel, Warthin and Dieterle—always with negative results.

Changes in the Spinal Cord.—Changes were present in the customary areas of the posterior columns, in which the tract either of Burdach

Fig. 2.—Island-like degeneration of the posterior columns; the islands of sclerosis are bordered by well preserved axons; an island under higher magnification is pictured in figure 4. Bielschowsky stain counterstained with the method of Alzheimer-Mann; × 140.

or of Goll was selectively involved, depending on the height and the extent of the lesion of the posterior roots. Even with the method of Weigert-Pal the pale, degenerated portions showed a number of practically normal myelinated fibers. These were especially numerous in sections stained with the method of Bielschowsky (fig. 2). This

revealed some nerve fibers practically unchanged; some possessed a swollen myelin sheath, which was present in some nerve fibers only in the form of fragments (that is, they were only partially covered with myelin), while in some nerve fibers the myelin appeared as globules, drops or droplets scattered alongside the preserved axons. In many instances the myelin globules were enclosed within vacuoles (fig. 3) which often contained gliogenous cells such as myelophages, myeloclasts and various types of glitter cells. A number of nerve

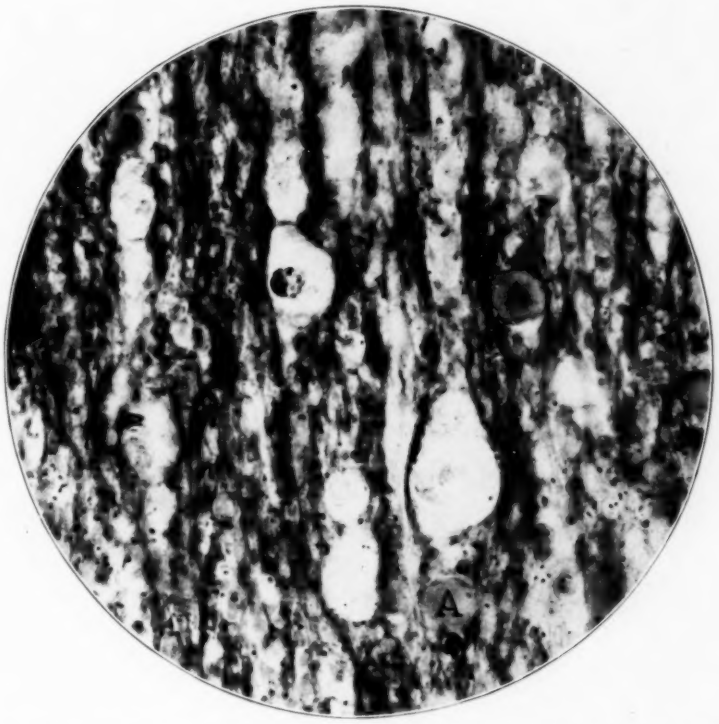

Fig. 3.—Longitudinal section of the posterior columns, showing vacuoles containing broken up myelin and other formations described in the text; *A.A.* are amyloid bodies, the upper enveloped by a glia fiber. The majority of the nerve fibers are swollen; the numerous dots are sections of glia fibers, represented in larger numbers in a transverse section of the cord. Bielschowsky stain; × 600.

fibers did not show myelin at all and appeared as naked axons. The axons were generally better and longer preserved than the myelin and were present even in the islands (fig. 4). They often appeared twisted, curled or in the form of a zigzag, and in rarer instances they were thinned or broken up into granules or minute droplets, sometimes enveloped by particles of broken up myelin. Some areas in the posterior

columns did not show traces of nerve fibers. They were composed of bundles of glia fibrils interspersed with glia nuclei which filled up the spaces between the healthy nerves and replaced the ones destroyed. In transverse sections the visual fields were thickly covered with minute dots (fig. 5), especially when stained with the methods of Alzheimer-Mann, Mallory-Jakob or Bielschowsky. The general aspect of the

Fig. 4.—Naked axons of an island; they are thinned and some are granular and broken up. The rest of the island is represented by sclerotic fibrillary glia tissue. Bielschowsky stain; × 650.

posterior columns stained with the foregoing methods was that of a degeneration in the form of spots or islands, or of "sclerosed islands" as Nageotte called them. I consider such an island-like degeneration of the posterior columns typical of tabes dorsalis. In cases of longer durations such areas were exceedingly vascular; they were covered with a

large number of blood vessels, the walls of which were thickened, hyperplastic and occasionally infiltrated with lipoid substances.

Excessive vascularity was present also in the lateral and anterior columns, but here the degenerative phenomena were confined to single or small groups of nerve fibers; that is, the apparently normal lateral and anterior columns also showed degenerative phenomena which were similar to those seen in the posterior columns. In general, they were sparse and mild. In the white columns numerous small vacuoles

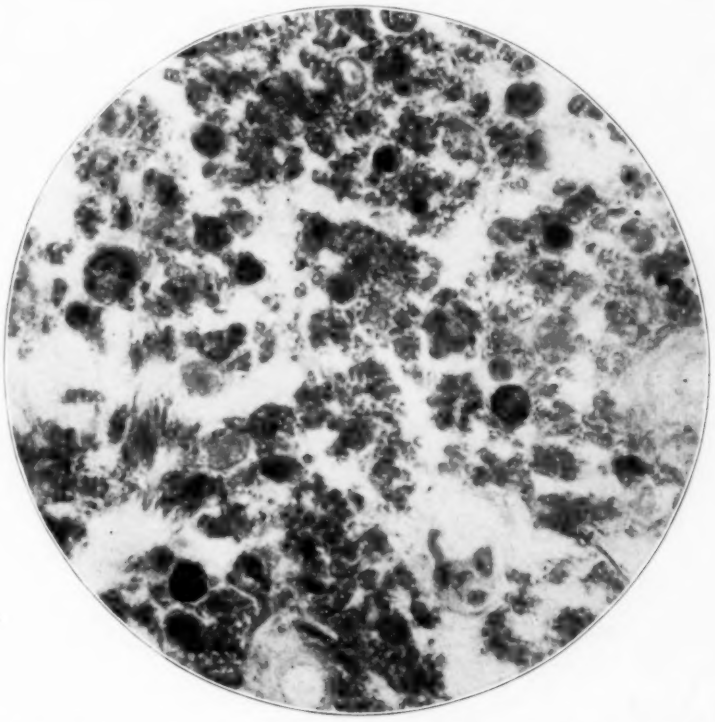

Fig. 5.—Transverse section of the posterior columns. The numerous dots are transversely cut glia fibers; some of the round bodies are amyloid bodies; the majority are glia nuclei. Alzheimer-Mann stain; × 1,200.

were present and gave the sections a sievelike appearance (fig. 6). They often formed small islands of rarefaction, which were especially marked in the posterior columns. Some vacuoles contained amyloid bodies which were scattered in large numbers over the white matter, especially of the posterior columns. Here they were numerous at the marginal glia, as if they had been washed over to this region, and they were also present within the meshes of the pia. Other vacuoles contained a broken up homogeneous substance and were adjacent to large glia nuclei rich in

chromatin. Many vacuoles, again, were entirely empty and showed no reactive phenomena; they were irregular in shape and their walls were torn (artefacts).

The degenerative phenomena described were associated with inflammatory reactions. These were present in the pia and sometimes also in its spinal cord prolongations, the septums. In some cases they were in evidence even in the area of Obersteiner-Redlich and often also involved the pial blood vessels. In general, the pial changes resembled those of syphilitic leptomeningitis.

Fig. 6.—Sievelike appearance of the posterior columns. Hematoxylin-eosin stain; × 120.

Changes in the Posterior Roots.—Like the posterior columns, the posterior roots revealed, in sections stained with the methods of Weigert-Pal or of Alzheimer-Mann, a scarcity of nerve fibers (fig. 7), the majority of which were replaced by scar tissue. Some nerve fibers were thinned, that is, reduced in volume; some, in contrast, were swollen and scattered among numerous blood vessels which were hyperemic, their walls often infiltrated with lymphocytes and plasma cells. The foregoing changes were marked in the so-called arachnoid portion of the

posterior roots. This runs (fig. 1) within the subarachnoid space, extending from the end of the posterior horn to the dural sac where it is continuous with the radicular nerve of Nageotte. In advanced cases the arachnoid portion of the posterior root was represented by a sclerotic neuroglia tissue enclosing a few preserved nerve fibers and blood vessels (fig. 8). It did not exhibit other signs of nerve degeneration and did not show the wealth and the variety of changes seen in the intraspinal segment of the posterior roots.

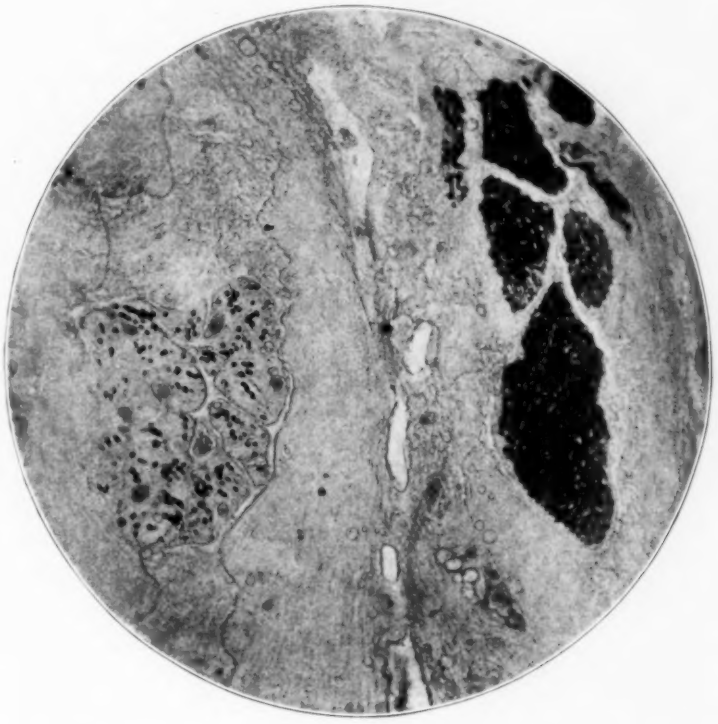

Fig. 7.—The posterior roots to the left show only a few normal nerve fibers, stained dark, in contrast to the well preserved anterior roots to the right. Weigert-Pal stain; × 40.

The nerve changes were much less in evidence in the ganglionic portion of the posterior root. This part, as pointed out, extends from the subarachnoid space (fig. 1) to the spinal ganglion. With the concomitant anterior root it forms what Nageotte [22] termed the "radicular

22. Nageotte, J.: Pathogénie du tabes dorsal, Presse méd. **10**:1179 (Dec. 10) 1902; **11**:5 (Jan. 3) 1903.

nerve." The fibers of the latter were normal in all my cases; I found in them no such signs of nerve degeneration as marked swelling or fragmentation of the myelin, changes in the axons or in the cells of Schwann. Instead of parenchymatous changes, there was a wealth of mesenchymal changes. As figure 9 shows, the numerous fasciculi that make up the nerve of Nageotte, or rather its sensory portion,

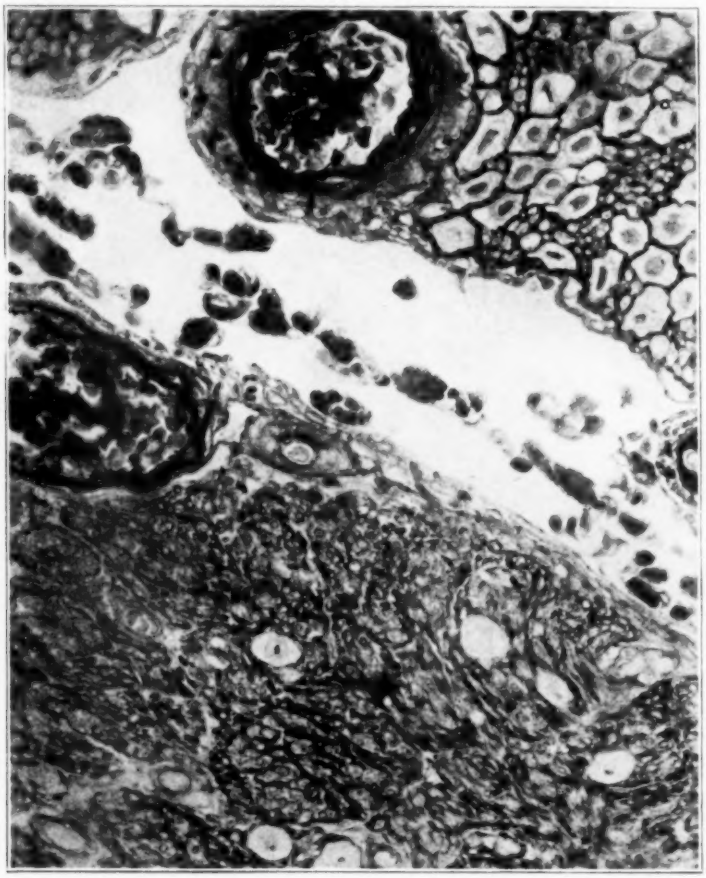

Fig. 8.—The fibers of the anterior root above show well preserved myelin and axons, and a patent artery divided from the posterior root by the arachnoid. The posterior roots below show only a few nerve fibers preserved; many fascicles are sclerosed; in the lower left corner is a large vein with a small artery to the right, both blood vessels belonging to the pia. Alzheimer-Mann stain; × 420.

exhibited perineural nuclear infiltrations (*Inf.*). These were sometimes dense and for the most part were confined to the marginal areas of the fasciculi (fig. 9 *F*). In other instances, the nuclear infiltrations were rather mild. The nuclei were oval or round in shape and varied in

size; they were pale and poor in chromatin, with no cytoplasm or processes and differed in no way from the so-called mesothelial cells of the arachnoid membrane. Stripped from the posterior roots and stained in toto, the latter normally shows a wealth of trabeculae. Crossing and recrossing the subarachnoid space, trabeculae give the latter the aspect of a dense sponge and, as shown by Key and Retzius,[23] they are covered by endothelial or "membrane" cells (Häutchenzellen). In this country they are termed (Weed, Essick) mesothelial, a view not shared by Maximow.[24] Probably it would be proper to call them arachnoid.

Fig. 9.—Fasciculi (*F.F.F.*) of a posterior root bordered by infiltrated (*Inf.*) perineural space; *Ps*, arynaceal or psammoma body; *Ar.*—arachnoid membrane. Hematoxylin-eosin stain; × 45.

Even in normal cords they form clusters, which in tabes are dense and quite numerous (fig. 10) around the posterior portion of the spinal cord. In sections of Nageotte's nerve, they appear as scattered cell

23. Key, A., and Retzius, G.: Studien in der Anatomie des Nervensystems, Arch. f. mikr. Anat. **9**:308, 1873.

24. Maximow, A.: Bindegewebe und blutbildende Gewebe, in Möllendorf: Handbuch der mikroskopischen Anatomie des Menschen **2**:315, 1927.

foci among the fasciculi of the posterior roots. In abnormal conditions of the spinal cord these cells are active and proliferated. Figure 11, for instance, shows Nageotte's area in a patient with Recklinghausen's disease. The similarity to figure 4 (tabes) of Richter [25] is great. In tabes they are the principal elements that pack, and often obliterate, the perineural (Richter's perifascicular) root spaces situated between the root fascicles and the arachnoid membrane. As numerous fasciculi are assembled in a comparatively small area in the nerve of Nageotte, the

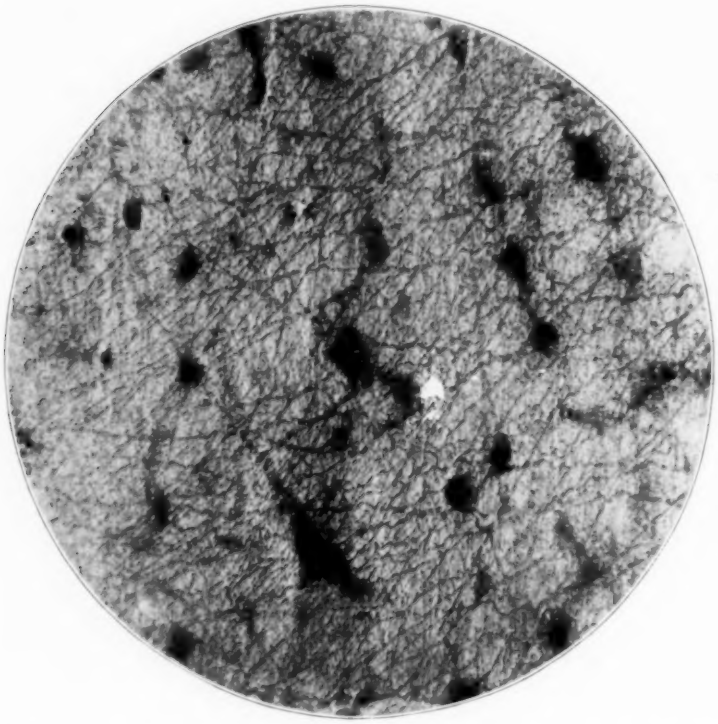

Fig. 10.—A stripped arachnoid from a case of tabes; the crossing and recrossing trabeculae are covered with dense dark masses or clusters or mesothelial cells of the arachnoid. Hematoxylin-eosin stain; ×45.

perifascicular infiltrations become particularly conspicuous. They are often mixed here with psammoma bodies (corpora arynacea) and hematogenous elements, such as lymphocytes, plasma cells and polyblasts.

In some cases the arachnoid appeared hyperplastic (fig. 13) and thickened, and surrounded the posterior root in the form of a broad

25. Richter (footnote 8, first reference).

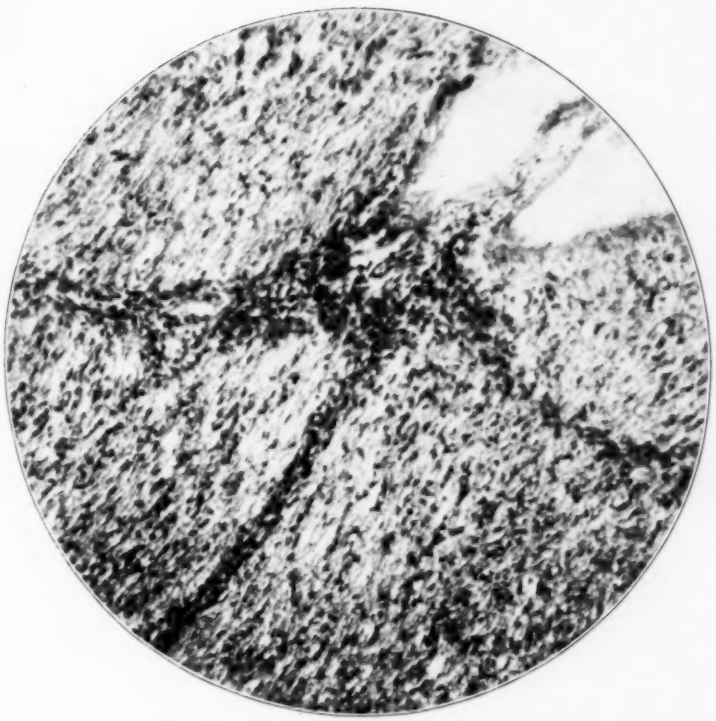

Fig. 11.—Nageotte's area from a case of Recklinghausen's disease. Other explanations are given in the text. The cells are reproduced under higher power in figure 12. Hematoxylin-eosin stain; × 140.

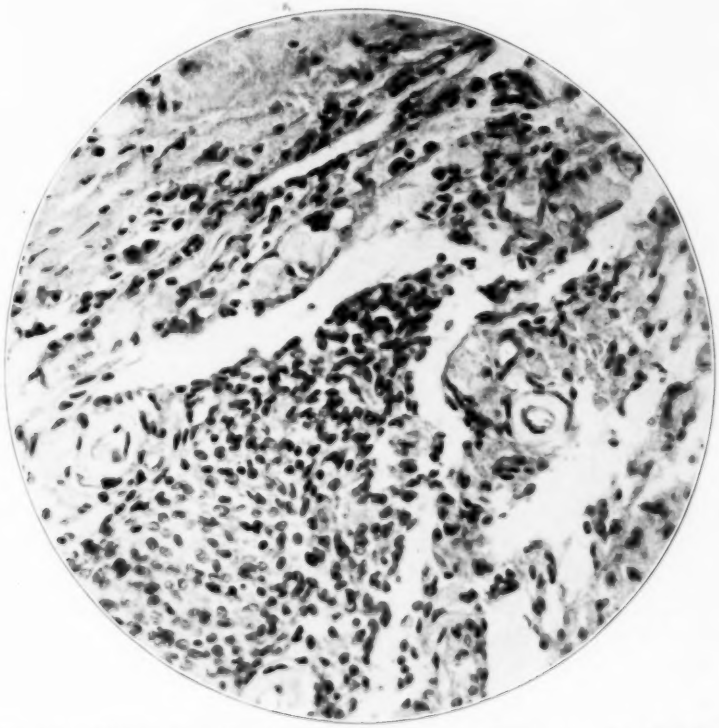

Fig. 12.—Higher magnification of cell masses in figure 11. Explanations are given in the text. Hematoxylin-eosin stain; × 300.

connective tissue band. Sometimes it appeared as if blended with the superimposed dura, obliterating the subdural space (fig. 13). In other instances the arachnoid protruded into the dura (fig. 14), nests of arachnoid cells invading the latter and thus contributing to the obliteration of the subdural space. In short, the membranes investing the posterior roots and individual fasciculi were often infiltrated and hyperplastic, and obliterated the subdural as well as the subarachnoid spaces of the posterior roots.

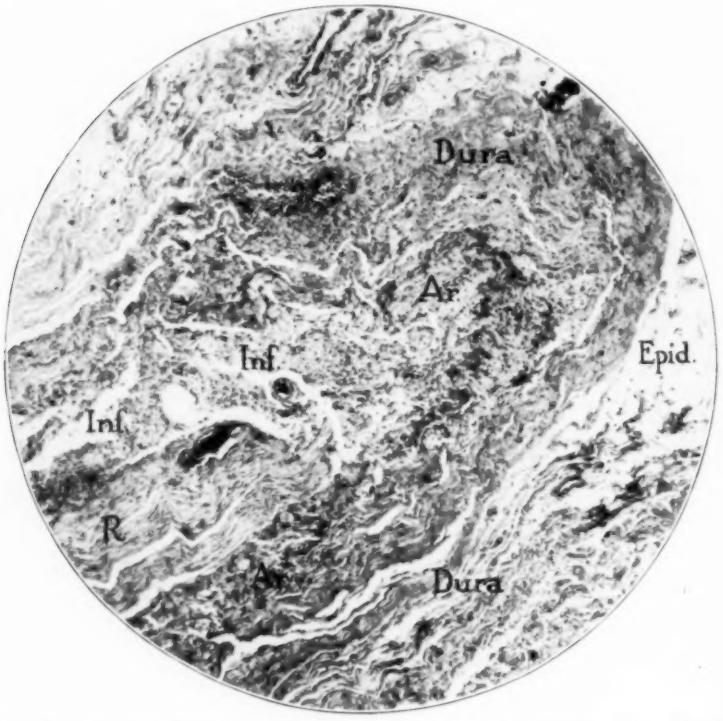

Fig. 13.—A root fascicle (*R*) surrounded by an infiltrated perineural (perifascicular) space (*Inf.*); the infiltration cells are similar to those of figures 11 and 12; the perineural space is surrounded by a hyperplastic arachnoid (*Ar.*) and dura. On the right the arachnoid adjacent to the dura is covered with masses of cells which, here, entirely obliterate the subdural space. *Epid.*, epidural space. Hematoxylin-eosin stain; × 65.

The changes of the anterior roots were rather meager. The intraspinal and subarachnoid segments, so markedly affected in the posterior roots, were entirely normal in the anterior roots, while in the area of Nageotte, in which the anterior roots participate in the formation of the radicular nerve, the arachnoid changes were mild and often absent altogether.

Changes in the Dura Mater.—In some instances there were diffuse infiltrations (fig. 15) of the dura with lymphocytes, plasma cells and polyblasts. The hematogenous dural infiltrations were sometimes in the form of dense circumscribed foci; others were as scattered inconspicuous groups of cells, or they were in the form of masses or nests of arachnoid cells. Sometimes the infiltrations within the dura were insignificant or even absent, but they were always in evidence epidurally, around the spinal ganglia and in their capsules. Here the epidural infil-

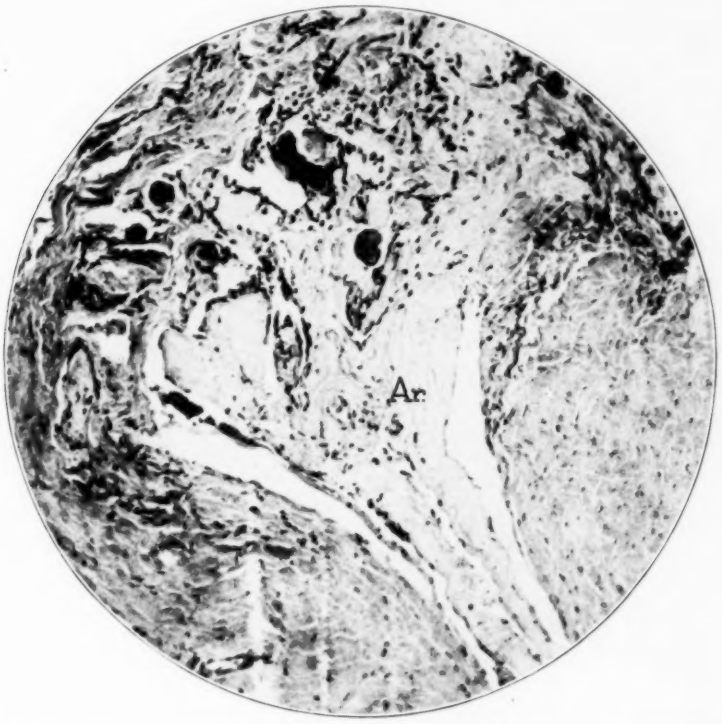

Fig. 14.—The arachnoid membrane (*Ar.*) is blended above with the dura; to the right and left it is separated from the latter by oblong empty subdural spaces which above are obliterated; the arachnoid contains several psammoma bodies and also shows scattered mesothelial or arachnoid cells. Van Gieson stain; × 110.

trations appeared as small scattered foci of cells; in some instances, however, they were dense, as in the dura itself (fig. 16). They either filled the meshes of the fatty connective tissue or were gathered around distended and hyperemic blood vessels. From the epidural spaces (fig. 17) masses of inflammatory elements extended to the dura, where they were mixed with proliferated fibroblasts. As said, they were also in evidence in the meshes of the capsule of the spinal ganglia as well as around the posterior roots.

Fig. 15.—Dura infiltrated with hematogenous elements. Hematoxylin-eosin stain; × 120.

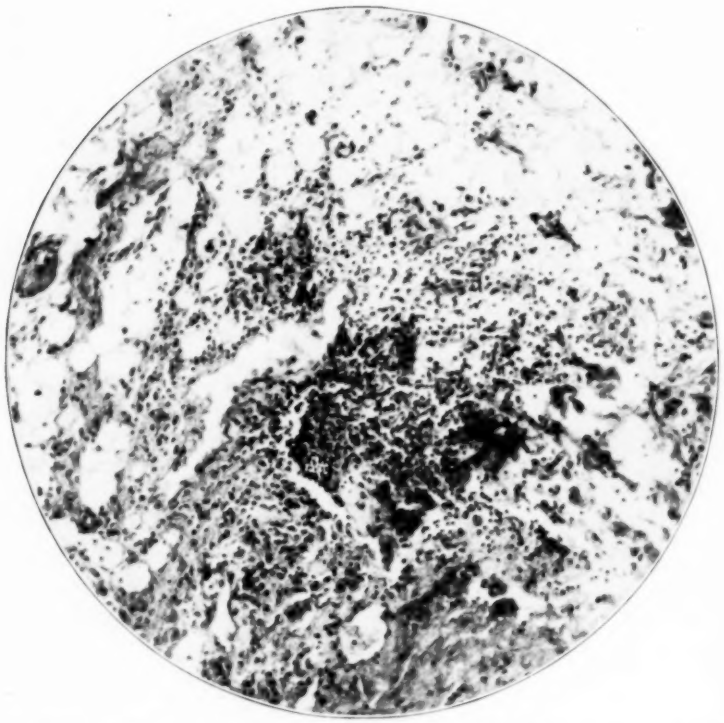

Fig. 16.—Epidural infiltrations with hematogenous cells. Hematoxylin-eosin stain; × 140.

The nerve cells of the spinal ganglia were more or less changed—they appeared excavated, vacuolated and often homogeneous; they contained masses of yellow pigment and exhibited marked phenomena of satellitosis and, occasionally, neuronophagia. Infiltration cells, as described in the area of Nageotte, were absent here.

Summary of Essential Pathologic Changes.—The essential pathologic changes consisted of island-like degeneration of the posterior columns of the spinal cord; scattered degeneration of single nerve fibers in the lateral and anterior columns; marked arachnoid (mesothelial) cell

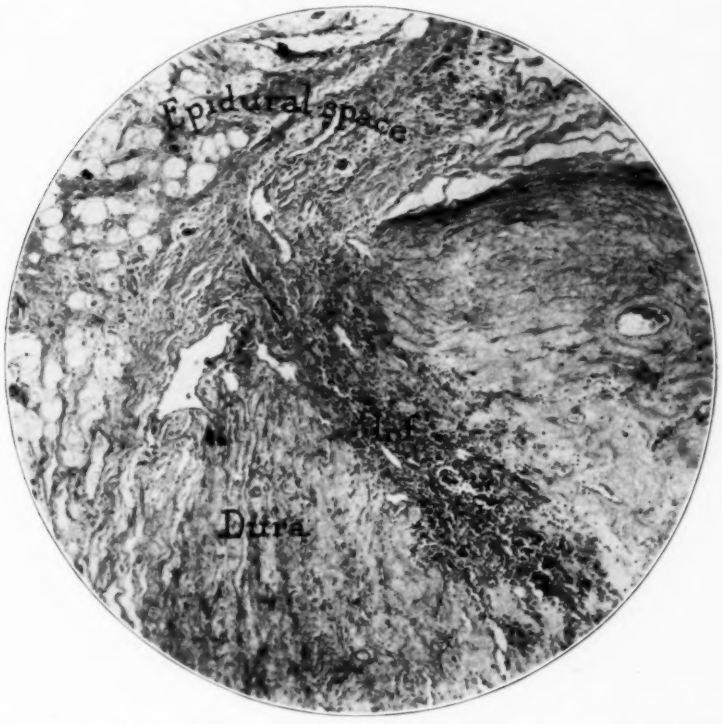

Fig. 17.—Invasion of the dura by masses of hematogenous elements (*Inf.*) from the epidural space. Hematoxylin-eosin stain; × 70.

infiltrations of the area or the nerve of Nageotte, with absence here of parenchymatous changes and the phenomena of leptomeningitis and peripachymeningitis.

COMMENT

The degenerative phenomena in the posterior columns were similar to those seen in multiple sclerosis, subacute combined degeneration of the cord and multiple neuritis. The degeneration was of so-called primary types for it originated in the nerve fibers themselves and was

independent of the condition of their trophic centers. As in the foregoing morbid states, the nerve fibers in tabes exhibited the various stages of nerve degeneration from the swelling and breaking up of the myelin to the ultimate wallerian degeneration of both myelin and axon. The only difference lay in the selective involvement in tabes of the posterior columns while the rest of the white matter was affected only slightly. If the degeneration of the posterior columns was a secondary process, caused, for instance, by strangulation of the posterior roots at the area of Obersteiner-Redlich or of Nageotte, the type of the degeneration and its stages or evolution would differ somewhat from what actually occurs in tabes. The degeneration would involve both the axon and the myelin at the outset as it does, for instance, in a peripheral nerve that has been cut or in some other manner divided from its trophic center. The infiltrations of the area of Obersteiner-Redlich or of the nerve of Nageotte may also contribute to the degeneration of the posterior roots,[20] but they are by no means important factors. Marked as the infiltrations may be, they are invariably confined to the margins of the single fascicles of the roots (figs. 9 and 13), and only in exceptional instances do the infiltration elements, whether hematogenous, embryonal (Nageotte), granulation (Richter), fibroblasts (Schaffer), or arachnoid cells, invade the fasciculi themselves (fig. 18). At any rate, even if they do penetrate the fasiculi, they are not sufficiently powerful or abundant to effect the destruction of the nerve fibers. The lack of intimate contact (Spitzer) between the infiltration cells and the root fibers, as well as the absence of distinct signs of their interruption, makes the mechanical or strangulation theory of the extraspinal origin of tabes not wholly acceptable.

The degeneration of the posterior columns must be considered a primary process which originates within the spinal cord itself. In this respect the view offered here conforms with the endogenous theory of Strümpell, Spielmeyer and others. My theory also explains well not only the phenomena of primary degeneration but the areas of rarefaction, the scattered vacuoles and the islands of degeneration. It is true that some of the changes, such as vacuoles and areas of rarefaction, are not conspicuous, especially in cases of tabes of long duration studied with the method of Weigert-Pal and its modifications. However, in suitably stained sections (hematoxylin and eosin, toluidine blue and thionin) such changes may be found not only in the posterior but in the lateral and anterior columns, being, like the islands, not artefacts but the results of nerve degeneration.

As pointed out in the introductory remarks, the toxin theory fails to give a satisfactory explanation for the posterior root degeneration; it does not explain the so-called local tabetic signs, such as the invariable

lesion of the so-called entrance root zone, nor does it explain the marked changes in the meninges.

Of meningeal changes, the best known and studied are those in the pia in the form of an acute or subacute inflammation. The pial blood vessels are sometimes infiltrated with lymphocytes and plasma cells. In some cases the infiltrations, as emphasized by Schroeder,[26] follow the blood vessels into the spinal cord not only in the posterior but also in the lateral and anterior columns, and the blood vessels often exhibit phenomena of endarteritis. In general, the aspect of the changes in the

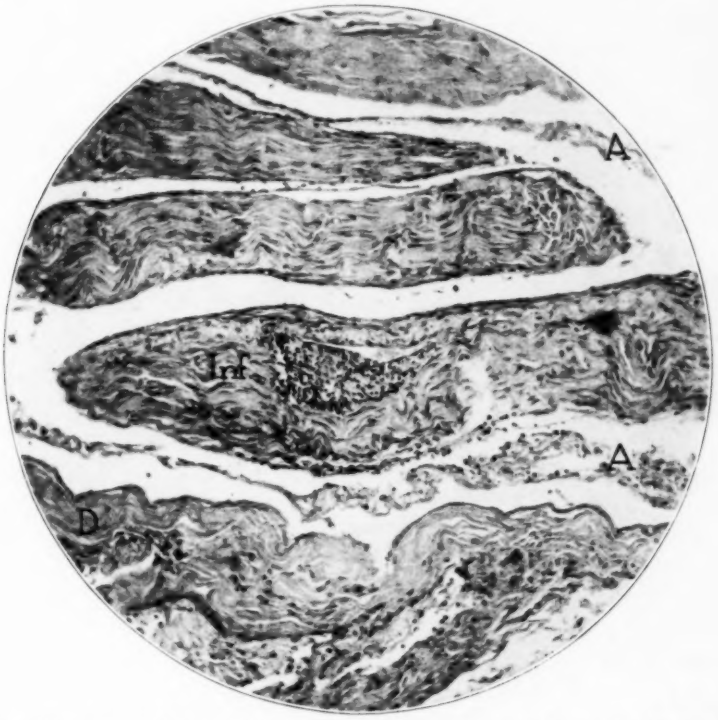

Fig. 18.—The middle fascicle contains in the center a focus (*Inf.*) consisting of mesothelial or arachnoid cells which are also scattered at the margin. *A*, arachnoid membrane; *D*, dura.

pia and its blood vessels is that of a syphilitic meningitis. In some cases this may be more, in some less marked, but it was present in all the cases I studied.

Of much greater interest and importance were the meningeal phenomena in the posterior roots, especially in that portion which is

26. Schroeder, P.: Ein Beitrag zur Histopathologie der Tabes Dorsalis, Centralbl. f. Nervenh. u. Psychiat. **29**:585, 1906.

known as the radicular nerve. This nerve does not possess a pial membrane but is covered by the arachnoid tunic, from which it is separated by the subarachnoid or perineural space (fig. 1). The arachnoid membrane in its turn is separated from the dura by the subdural space. Though large around the spinal cord, these spaces become greatly narrowed over the radicular nerve. As figure 1 shows, even here they are not closed spaces obliterated by a fused dura-arachnoid, as Richter thought, but are patent formations, continuous with the spinal subdural and subarachnoid spaces. According to Key and Retzius,[27] they are continuous with similar spaces of the peripheral nerves and even with the tissue spaces of the spinal cord itself. As was convincingly demonstrated by their famous injections, the spinal fluid flows from the spinal cord to the subarachnoid space and from the latter by way of the perineural root spaces to the peripheral nerves. In tabes many of the perineural root spaces are obliterated by arachnoid cells (figs. 9 and 13). The avenues of escape of the cerebrospinal fluid thus become obstructed. The result is stagnation of the tissue fluids in the spinal cord, especially in the posterior columns. This leads, in early stages, to the formation of vacuoles, areas of rarefaction, phenomena of primary nerve degeneration and formation of islands of degeneration. In advanced stages, glia scar tissue is the result.

The preeminent involvement of the posterior columns is due to the fact that their drainage is evidently accomplished mainly by the perineural spaces of the posterior roots, which in tabes, as noted, are for the most part obliterated. Any other obstruction to the escape of the spinal fluid—for instance, by an epidural abscess or a tumor—may cause changes in the cord similar to those of tabes. The areas of rarefaction seen in the posterior and other columns in figure 19 were caused by a large epidural granulation mass which enclosed three well defined abscesses. In this case the obstruction of the perineural spaces (fig. 20)—by hematogenous elements—was greatest at the level of the mass. Accordingly, the changes in the cord were most pronounced at this level. Above and below the epidural mass they were absent, for at these levels were also absent the epidural phenomena, which might have caused obstruction of the perineural spaces as well as obstacles to the outflow of the cerebrospinal fluid, or, which is the same of the tissue fluids of the spinal cord. The involvement of additional areas (lateral and anterior columns) was due to the fact that in this case the epidural changes extended over a larger circumference of the cord, thus causing a more extensive obstruction.

27. Key, A., and Retzius: Studien in der Anatomie des Nervensystems, Stockholm, 1876, vol. 2, p. 68.

A similar interpretation also renders clear the changes observed in the spinal cord in persons with epidural tumors and, as shown elsewhere,[28] in cases of increased epidural pressure produced experimentally. Clear and comprehensible as such a relationship is in persons with epidural tumors, abscesses and similar conditions, it is much less so in those with tabes in whom the epidural phenomena and their effect on the roots and the spinal cord are much less evident and, therefore, less comprehensible or even obscure. Being mainly inflammatory, the epidural changes directly or indirectly involve the dura and the subjacent pia-arachnoid.

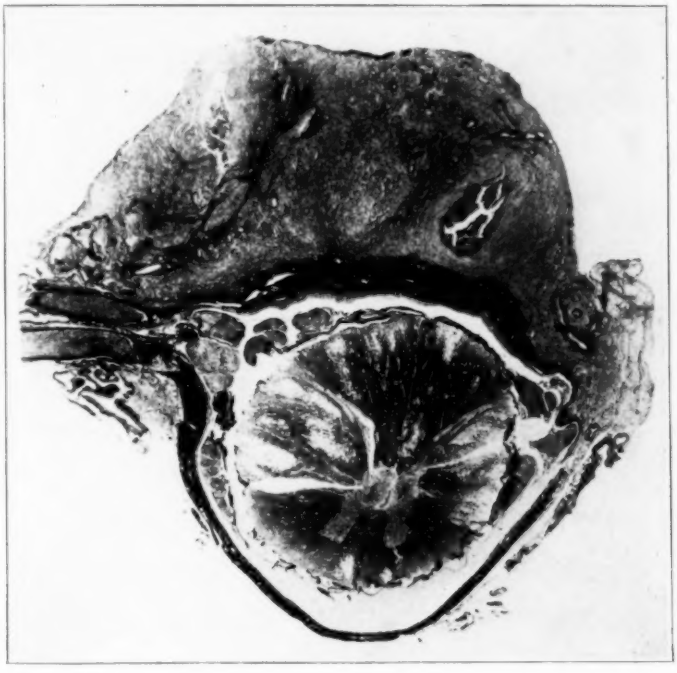

Fig. 19.—Epidural granulation tissue enclosing abscesses. The broken down areas in the posterolateral columns of the spinal cord are marked. Van Gieson stain.

The pia, which is rich in blood vessels, responds by perivascular infiltrations while the arachnoid, being avascular, responds by proliferation of the arachnoid (mesothelial or "granulation") cells which obstruct the perineural spaces and cause the changes in the roots and cord previously described. An inflamed epidural space may thus affect the subjacent avenues of escape of the cerebrospinal fluid, either by direct pressure

28. Hassin, G. B.: Circumscribed Suppurative (Nontuberculous) Peripachymeningitis, Arch. Neurol. & Psychiat. **20**:110 (July) 1928.

(as in tumors) or indirectly by exciting in them an inflammatory reaction (as in tuberculosis and syphilis). The effect in both instances is the same. The difference is only in the type of the changes produced which also may be due to the time element. For this reason changes seen in the spinal cord, for instance in epidural abscess, may be considered early or initial manifestations of what occurs in tabes, in which they are usually late.

Fig. 20.—Epidural abscess. Obliteration of the perineural spaces by masses of hematogenous elements. Toluidine blue stain.

The two outstanding phenomena in tabes—the intraspinal degeneration and the extraspinal inflammation—are thus closely associated. The changes which occur first and are of paramount importance are evidently the extraspinal—inflammation of the epidural and intradural spaces; obstruction of the perineural root spaces with its effects on the spinal cord is most likely secondary, additional or accidental; the changes in the spinal cord itself are the latest to appear and the least important.

The essential phenomenon is therefore invasion of the posterior epidural space by a specific infection. When the latter is syphilis, the inflammatory reaction may result in three conditions: tabes, syphilis of the cord or paresis. In the last two conditions the reaction in the epidural tissues and the subjacent areas differs from that in tabes: it is more pronounced and is represented preferably by a mass of hematogenous cells. Figure 21 shows the reaction of the epidural space in syphilis of the spinal cord; figure 22 shows the condition of Nageotte's nerve

Fig. 21.—Syphilis of the cord. The three dark streaks (artefacts) point to the margin dividing the dura from the epidural space. This is greatly infiltrated and contains a number of blood vessels; their walls, especially the adventitia, are infiltrated. Hematoxylin-eosin stain; × 40.

in paresis. In both instances the infiltrations are immense, consisting mainly of lymphocytes and plasma cells, while the arachnoid (mesothelial) cells are few, in contrast to what is seen in pure, uncomplicated tabes. Such a difference in the reaction of the epidural space in three conditions possessing the same etiology is of great biologic significance. In persons with paresis and syphilis of the cord, the epidural reaction leads to infiltration of the perineural root space

with hematogenous cells; in persons with tabes, the perineural space is infiltrated with arachnoid cells. Blocking of the perineural root spaces with the latter shuts off the spinal cord from a possible invasion or contamination by the syphilitic infection, and for this reason probably a tabetic cord does not show syphilitic changes. In taboparalysis and syphilis, the invading hematogenous elements (lymphocytes, plasma cells and polyblasts) are evidently not sufficiently powerful to effect an occlusion of the perineural spaces and thus to prevent the infection from enter-

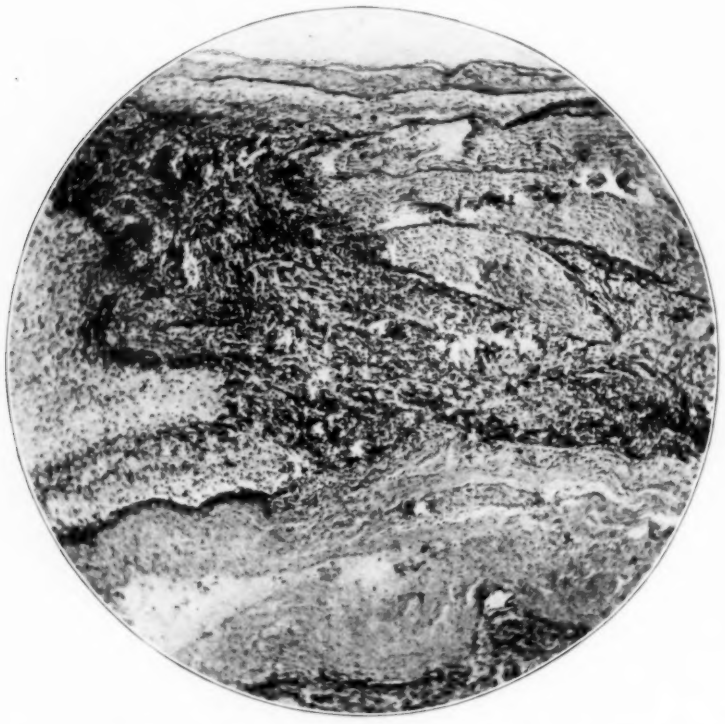

Fig. 22.—Paresis. The infiltration masses are all within the area of Nageotte and consist of lymphocytes, plasma cells and other elements. Van Gieson stain; × 40.

ing the central nervous system. Such a difference in the reaction may be due to the severity of the infection, to the difference in the organism's resistance and, as is probably more significant, to the time element. Since taboparalysis and syphilis of the spinal cord possess, in contrast to tabes, a less chronic course, being mainly subacute diseases, the epidural and other changes in these conditions may also be considered subacute, probably as early stages of what generally takes place in tabes. In tabes the reactive phenomena represented by the arachnoid (mesothelial)

cells and few hematogenous elements are chronic, the reverse of what occurs in syphilis and taboparalysis.

The views here outlined differ from those generally advocated even by the latest investigators (Richter, Sven Ingvar, Spitzer and others). Richter justly insisted that the pathologic changes of tabes should be studied only in cases that are not complicated by paresis or syphilis of the cord, for uncomplicated cases of tabes ordinarily do not show hematogenous elements in the radicular nerve of Nageotte. Richter expressed the belief that the tabetic infiltration cells, which he termed "granulation," originate in the lymph spaces of the dura. Here the spirochetes land from the spinal fluid—which, according to Richter, is spirochetal—and provoke a tabetic reaction in the form of proliferation of the endothelial cells and their invasion of the "perifascicular" spaces. In early cases the "granulation" cells are at the periphery; in old cases they invade the tissues as fibroblasts and as sclerotic connective tissue. They invade first transversely; when inside, they spread longitudinally, causing secondary degeneration of the cord. The latter is also due to the toxic spirochetal fluid which is in much closer contact with the posterior than with the anterior roots. For this reason, it causes a more marked degeneration of the former. The lumbar roots are, according to Richter, affected because they run vertically and the spirochetes become "sedimented," sinking by gravitation into the pouches of the meninges and causing connective tissue proliferation. In three of nine cases of pure tabes, Richter found spirochetes in the granulation tissue of the nerve of Nageotte.

In one of his shorter contributions on the pathogenesis of tabes,[29] Richter spoke of three stages: invasion of the root funnels ("entonnoirs radiculaires") by spirochetes; proliferation of granulation tissue caused by it, and the ultimate destruction of the root fibers.

It is needless to say that some of Richter's statements are based on hypotheses. For instance, the "spirochetosis" of the spinal fluid has not been proved; nobody has demonstrated the presence of spirochetes in the cerebrospinal fluid.[30] Lymphatics have not been demonstrated in the radicular nerve or its meninges, nor has strangulation of the root nerve by invasion of connective tissue. As to the sinking of the spirochetes as if they were lifeless bodies—their sedimentation—Richter himself did not entertain such a view seriously. As to the "granulation" cells, they are not specific for tabes, for as noted they occur also in nontabetic cords (fig. 11). The difference is that in tabes they are not as a rule confined to one level, but are scattered throughout the entire length of the spinal cord, appearing at many levels. However, the basic idea of

29. Richter (footnote 8, third reference).

30. Jeanselme, E.; Schulman, and Martin: Presse méd. **33**:1041, 1925.

Richter that the invasion of the perineural (perifascicular) root spaces is not by hematogenous elements is correct. The disagreement is as to the effect of such infiltrations on the degeneration of the root and cord. Richter saw the effect in the ultimate formation of connective tissue and subsequent strangulation and degeneration, while the view that I advocate here is that the infiltrations block the perineural spaces, interfere with the outflow of the cerebrospinal fluid and produce a consequent degeneration of the cord and root. The entry of the infection is, according to Richter, from the spinal fluid; according to my conception, it is from the epidural space. Becoming here anchored, as it were, the syphilitic infection with its resulting inflammation sooner or later affects the subjacent dura. When of long duration it also extends to the subdural and subarachnoid root spaces and causes their obstruction. The selective localization of the infection in the posterior epidural space (and posterior roots) thus explains why the posterior columns are involved in tabes in preference to the lateral and anterior portions of the cord. It also explains a number of clinical manifestations. Shooting pains, disturbances of sensibility, crises and other sensory phenomena may be explained by involvement of the spinal nerves in the epidural space.

Changes in the epidural space may give symptoms and signs of tabes even in the absence of changes in the root or spinal cord and vice versa. For instance, in Spitzer's case the clinical picture was that of polyneuritis while the pathologic condition was that of tabes. In the case of André-Thomas and Hauser [31] with a clinical picture of advanced tabes, hardly any pathologic changes were present in the cord; they were even less marked than in so-called tabes "fruste." Cases of so-called pseudotabes or peripheral tabes also show that a clinical picture of this disease may be caused by a nontabetic condition. On the other hand, Pitres and Vaillard [32] found extensive peripheral nerve lesions (neuritic) in the lower extremities in seven persons with tabes dorsalis. These authors referred to Oppenheim and Siemerling who found, in eight of thirteen cases of tabes, notable changes in the peripheral nerves. These were degenerative, in the form of fragmentation of the myelin and a granular breaking up. Pitres and Vaillard asserted that tabetic symptoms may be complicated by neuritic symptoms such as patchy anesthesia, analgesia, paresthesia, hyperesthesia, persistent pain, trophic lesions of the skin and some muscular atrophies and palsies, as well as crises and fractures of the bones. In contrast, peripheral nerve lesions, they

31. André-Thomas, and Hauser, G.: Tabes avec lésions à peine appreciable de la moelle, Rev. neurol. **14**:573, 1906.

32. Pitres, A., and Vaillard: Contributions à l'étude des névrites périphériques chez les tabétiques, Rev. de méd. **6**:574, 1886.

stated, do not play a rôle in the causation of specific symptoms, such as loss of tendon reflexes, shooting pains, ataxia and disturbances of muscle sense.

Dejerine,[33] in his early publications, also emphasized the implication of the peripheral nerves in tabes and even defined it as a peripheral nerve disease. Nageotte [34] Pierret,[35] Raymond,[36] and many others described changes in the peripheral nerves in tabes. Leyden [37] stated that there is much in favor of the view that tabes originates at the periphery and that he was prone to accept such a view though it was hard, as he said, to understand how a morbid process can extend from the peripheral sensory nerves to the spinal cord over the spinal ganglia and the posterior roots.

The pathologic phenomena here outlined and the facts pertaining to the pathogenesis of tabes seem to be in accord with the view that the "seat" of tabes or the main origin of the "tabetic changes" are outside the spinal cord and in the epidural space. The favorable results from the treatment with epidural injections [38] also seem to favor such a view.

In conclusion, I wish to state that pathologic studies of tabes cannot be regarded as complete without a careful study of the epidural space, including the periosteal dura as well as its contents—the spinal nerves at their origin before they enter the intervertebral foramens and the blood vessels. As such studies could not be carried out in detail and will be recorded at some future time, this report is considered preliminary.

CONCLUSIONS

1. The histologic changes in tabes dorsalis may be classified as degenerative and inflammatory.

2. The degenerative changes involving the posterior columns and the arachnoid portion of the posterior roots are a primary process due to disturbed circulation of the tissue fluids in the spinal cord, especially in its posterior columns.

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33. Dejerine, J.: Des altérations des nerfs cutanés chez les ataxiques, de leur nature périphérique, et du rôle joué par ces altérations dans la production des troubles de la sensibilitité que l'on observe chez ces malades, Arch. de physiol. norm. et path. **15**:72, 1883.

34. Nageotte, J.: Étude sur la méningo-myélite diffuse dans le tabes, la paralysie générale et la syphilis spinale, Arch. de neurol. **30**:273, 1895.

35. Pierret: Nouvelles recherches sur les névrites périphériques observées chez les tabétiques vrais, Compt. rend. Acad. d. sc. **102**:1581, 1886.

36. Raymond, F.: Sur la topographie des lésions spinales du tabes au début, Rev. neurol. **11**:1, 1891.

37. Leyden, E.: Die neuesten Untersuchungen und die pathologische Anatomie und Physiologie der Tabes, Ztschr. f. klin. Med. **25**:1 and 181, 1894.

38. Hassin, G. B.: Treatment of Tabes Dorsalis by Epidural Injections of Neoarsphenamine: Preliminary Report, J. A. M. A. **90**:605 (Feb. 25) 1928.

3. The inflammatory changes occur in the dura and the pia-arachnoid, in which they provoke reactive phenomena. In the dura they occur as infiltrations with hematogenous elements and vascular changes typical of syphilis; in the arachnoid they appear as proliferation of the cells of the arachnoid (arachnoid or mesothelial cells). These are most likely what Richter designated as "granulation" cells.

4. The arachnoid cells invade the perineural spaces, obstruct them and thus interfere with the flow of cerebrospinal fluid from the subarachnoid space, indirectly causing phenomena of stasis in the spinal cord.

5. The stasis results in rarefaction of spinal cord tissue and its ultimate sclerosis, which shows as islands of degeneration in the posterior columns.

6. The pia-arachnoid phenomena are secondary to the distinctly inflammatory conditions of the dura and the epidural space; invading the subjacent structures, they result in the changes mentioned in paragraphs 4 and 5.

7. The strangulation phenomena of Obersteiner and Redlich, Nageotte, Richter and others are contributory but are not the main factors.

8. Many clinical phenomena can be better understood on the basis of the epidural origin of tabes with involvement of the peripheral nerves in the epidural space.

9. Future studies of tabes should be centered on the epidural space, including both the spinal and the periosteal dura, as well as on the spinal nerves before they leave the intervertebral foramens.

ABSTRACT OF DISCUSSION

Dr. Harold G. Wolff, Boston: Which cells contain or have given rise to the vacuoles observed in the posterior columns, and is there any relation between this vacuolization and the stasis of cerebrospinal fluid?

Dr. Ferraro, New York: Dr. Hassin's paper is important, as it is one of the few dealing with the new conception as expressed by Richter and Schaffer in the pathogenesis of tabes. As a matter of fact, these authors described peculiar granulations which take place in the so-called radicular nerve of Nageotte. According to them the accumulation of these cells produces a strangulation of the nerve fiber, which is followed by degeneration in the posterior column. The degeneration in the posterior column is then a secondary one. The field of distribution of the degeneration in the posterior column corresponds indeed to the involved nerve root which forms this given area. I am glad that Dr. Hassin has investigated the presence of these cells because as yet there has been nothing in the literature dealing with this process, and I was puzzled as to the importance of the contribution of Richter. Dr. Hassin admits the presence of these cells but does not consider them as specific. I should like to ask him if he thinks with Richter and Schaffer that in the pure uncomplicated process of tabes strangulation

of the tissue may be the only cause to produce degeneration of the nerve fiber and if this occurrence may be independent of the infiltration of hematogenous cells. As a matter of fact, according to Richter, the pure process of tabes is a process in which hematogenous infiltration cells are lacking, the presence of infiltration meaning a complication of the process. Has Dr. Hassin ever seen such an uncomplicated picture? His conception that tabes is the result of primary degeneration of the posterior column, due to the presence of cerebrospinal fluid which lacks the possibility of escape following adhesions of the meninges, is worthy of serious consideration, and will actually open again a lively discussion between the partisans of the primary and secondary origin of lesions in the posterior column in cases of tabes.

Dr. Hassin: Concerning vacuolization, it is the result of stasis and the consequent nerve degeneration. The result is that the nerve fibers drop out and produce the vacuoles. The cells that Richter described as granulation cells do not cause strangulation of root fibers, according to my conception. Richter thought that they develop fibroblasts which turn into connective tissue and cause degeneration of Nageotte's root nerve. Even some admirers of Richter claim that this is not the case, for one usually sees accumulations of cells dividing the nerve bundles but not penetrating them. The perineural spaces are blocked by them and they ultimately become fibrosed or sclerosed and block the outflow of the cerebrospinal fluid. For this reason I demonstrated the pictures from a patient with general sarcomatosis, showing what occurs in the spinal cord when the outflow of spinal fluid is interfered with.

THE SUGAR CONTENT OF THE BLOOD IN EMOTIONAL STATES*

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For some time it has been a general opinion that the sugar content of the blood bears a definite relationship to the emotional state. The most important work on this theory is that of Cannon.[1] An exhaustive résumé of Cannon's views is unnecessary. Briefly, Cannon has conceived that in acute emotional states, such as fear, anger and rage, there is stimulation of the sympathetic nervous system, an increased secretion of epinephrine due to stimulation of the suprarenal medulla and that, among a number of physiologic effects resulting therefrom, there is a definite increase in the sugar content of the blood. According to Cannon, the reason for this increase of blood sugar is a protective one. In acute states of fear or anger, the organism needs more energy for flight or fight. Therefore, if sugar is mobilized in the blood and made available, this energy is ready for use.

Cannon's theory is based essentially on the following experiments:

> Twelve cats, which did not previously show glycosuria, were tied in a holder and became excited. Glycosuria resulted in all and was brought about in less than an hour and a half. Three cats were then bound in a holder. These cats did not show excitement as a result of the procedure and the urine collected subsequently did not show glycosuria. They were then barked at by a dog, which produced a response of excitement with rage or fear. Each cat, following the excitement, developed glycosuria. Cannon[2] assumed that the glycosuria was due to a hyperglycemia of sufficient degree to go above the normal threshold of kidney tolerance for sugar. To prove that the suprarenals were largely responsible for the hyperglycemia three cats were chosen which previously had shown glycosuria on excitement. The suprarenals were removed in these cats and then, in spite of a prolonged period of excitement, the cats did not show glycosuria.

This classic experiment of Cannon has been largely accepted as proof that extreme emotion produces an increase of the blood sugar.

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* Submitted for publication, June 19, 1928.

1. Cannon, Walter B.: Bodily Changes in Pain, Hunger, Fear and Rage, New York, D. Appleton & Company, 1920.

2. Cannon, W. B.; Shohl, A. T., and Wright, W. S.: Emotional Glycosuria, Am. J. Physiol. **29**:280, 1912.

Cannon and his co-workers also give the following experimental data as further proof of the correctness of this theory: They have determined the presence of epinephrine in the blood stream following emotional states. They have demonstrated that injections of epinephrine cause a rise of blood sugar. Considerable other work tending to corroborate this is not reported because of lack of space.

A number of other writers have reported glycosuria following emotional states. Smillie [1] found glycosuria in four of nine medical students following a hard examination, although all of them were normally without sugar in the urine. Following an easier examination, only one of the nine had glycosuria.

Fiske and Cannon [1] examined the urine of twenty-five members of the Harvard football squad immediately after the final and most exciting contest of the season and found sugar present in twelve. Five of these positive results were among substitutes not called on to enter the game. The only excited spectator of the Harvard victory whose urine was examined also had a marked glycosuria, which disappeared on the following day.

Folin, Dennis and Smillie [3] examined the urine of thirty-four medical students before and after examinations. One student had glycosuria before and after the examination. Of the remaining thirty-three students six, or 18 per cent, had small but unmistakable traces of sugar in the urine passed immediately after the examination.

These workers thought that women college students, being more emotional, would show a higher percentage of sugar in the urine, but this did not prove to be the case. Thirty-six sophomores at Simmons College were tested. Six students, or 17 per cent, had sugar in the urine after an examination.

As a result of their study, Folin and his co-workers came to the conclusion that "it seems reasonably certain from the results obtained that pronounced mental emotional strain may produce a temporary glycosuria in man."

In a later article, Folin and Berglund [4] attempted to account for the fact that in their experiments the blood sugar did not rise to the high level which practically all other investigators had obtained by similar experiments. They believed that the reason for this was that other experimenters had produced an emotional hyperglycemia, whereas they had used as subjects healthy medical students who had offered to serve

3. Folin, Otto; Denis, W., and Smillie, W. G.: Some Observations on Emotional Glycosuria in Man, J. Biol. Chem. **17**:519, 1914.

4. Folin, Otto, and Berglund, Hilding: Some New Observations and Interpretations with Reference to Transportation, Retention and Excretion of Carbohydrates, J. Biol. Chem. **51**:212, 1925.

and who knew that pain or danger was not involved in the experiment. In one case they found what they regarded as satisfactory proof of an emotional hyperglycemia.

> The subject, a medical student, never had sugar in his urine (qualitative tests) either before or after the day of the experiment. When the preliminary sample of blood was taken he grew pale and very faint. When the second sample was taken he fainted completely. The plasma of this blood sample contained 210 mg. of sugar, whereas the first contained only 105 mg. In the course of the next hour the sugar content sank to 111 mg. and neither at this time nor later did the taking of the blood disturb him. Glycosuria was present.

Cannon [1] also cited several German observers who noticed that in their patients diabetes followed some serious emotional situation, such as distressing experiences during the Franco-Prussian War or unfortunate love situations. He [5] also cited cases in which the condition was observed in aviators after a flight and in citizens after being subjected to the excitement of a bombardment.

Tigerstedt [5a] found sugar in the urine of ten of thirteen students after a six-hour examination. Nylander's test was used.

Bang [6] stated that hyperglycemia and glycosuria may occur as a result of various emotions. He did not report work of his own but quoted Cannon's experiments and the work of von Bolim and Hoffmann. Human beings show hyperglycemia and glycosuria after emotional stress, but they occur most frequently in persons with latent diabetes, which becomes manifest under these conditions. Bank quoted von Noorden, Fredricks and Teschemacher, who reported cases. Postoperative glycosuria may be due to emotion. On the other hand, he stated: "In contradistinction is the observation that on the operating table rabbits do not get any hyperglycemia or glycosuria in spite of the fact that they are definitely afraid and, for many hours, tied in a holder."

Feinblott [7] believed that transient hyperglycemia may result from emotional states, but he did not present data in support of this belief.

Maranon [8] reported hyperglycemia in aviators due to the emotion preceding flight. He found a still higher hyperglycemia after flight from the emotion of flying itself. Eight cases are reported of students flying for the first, second or third times or of new pilots or of pilots who had

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5. Cannon, Walter B.: New Evidence for Sympathetic Control of Some Internal Secretions, Am. J. Psychiat. **11**:1, 1922.

5a. Tigerstedt, C.: Die Blutdruck der Menschen bei pyschischer Exzitation, Skandin. arch. f. Physiol. **48**:138, 1926.

6. Bang, I.: Der Blutzucker, Wiesbaden, 1913, p. 51.

7. Feinblott, Henry M.: Hyperglycemia Based upon a Study of Two Thousand Blood Chemical Analyses, J. Lab. & Clin. Med. **8**:500, 1923.

8. Maranon, G.: Nota acerca de la influencia del vuelpo sobre la glucemia, Siglo med. **66**:573, 1919.

not flown for some time. As controls he used "two old pilots, well trained in flying." Before flight, they showed symptoms of emotion, such as motor excitation, overtalkativeness, slight tremor of the hands on extension, slight hypertension and increased pulse rate. After flight the emotion was increased as well as were also the tremor and hyperextension. In old pilots hyperglycemia occurred, even if the flight was easy, if they had an untrained man with them and had to observe him. The data are given in table 1.

Although Cannon and those agreeing with him appear to have established conclusively that glycosuria often follows an acute emotional state, there are few data on the actual amount of sugar in the blood. Cannon assumed that the glycosuria is on the basis of hyperglycemia as

TABLE 1.—*Sugar Content of the Blood in Relation to Aviation* *

	Before Flight					After Flight				
	Blood Pressure					Blood Pressure				
Case	Systolic	Diastolic	Pulse	Tremor	Blood Sugar	Systolic	Diastolic	Pulse	Tremor	Blood Sugar
1	180	110	68	+	150	200	120	64	+	120
2	190	100	72	+	160	210	80	92	+	190
3	100	50	84	+++	190	160	90	84	+++	180
4	180	90	80	+	190	210	90	80	+	190
5	200	100	60	+	100	210	100	88	0	160
6	190	90	76	+	130	220	80	84	+	150
7	170	90	68	+	130	160	80	72	+	180
8	200	130	80	+	150	210	110	88	++	160
9	170	90	104	0	100	170	70	108	+	150
10	210	110	92	+	120	190	110	88	+	200

* The pilots in cases 1, 2 and 3 were flying for the first time; the pilot in case 4 was flying for the second time, and the one in case 5 for the third time. The man in case 6 was an old passenger who had not flown for a long time. The subject in case 7 was a new pilot on one of his first flights, who had an accident but who came down quietly. The man in case 8 was an old pilot flying after a long rest. The men in cases 9 and 10 were old pilots who went up every day.

do all other writers, but except for the one case cited by Folin and Berglund and cases cited by Maranon reports of the sugar content of the blood have not been published.

In discussing this matter with us, Dr. Cannon was kind enough to give us the following further evidence of emotional hyperglycemia:

The figures which I referred to when you were here a few days ago were obtained last year for purposes of comparing the effects of emotional excitement on normal and on sympathectomized animals. The duration of excitement was, with only four exceptions, ten minutes. In six observations on normal animals, in which a modification of the Folin-Wu method was employed, the blood sugar before the excitement averaged 88 mg. per hundred cubic centimeters, with 74 and 96 as the extremes of variation. After the excitement the average was 114 mg. per hundred cubic centimeters—an increase of 26 mg. The variations were between 101 and 127 mg. In the case of 101 mg. per hundred cubic centimeters, the rise was from 74. If the cat has a kidney threshold of 170 mg., it is clear that in these cases there would have been no glycosuria. The hyperglycemia is, however, quite definite. In eight observations on sympathectomized animals the average

was 86 mg. per hundred cubic centimeters before excitement and 85 mg. per hundred cubic centimeters afterwards. It is clear that in the absence of sympathetic impulses the excitement has not had its usual effect.

Although this report by Cannon is to be regarded as important evidence of an emotional hyperglycemia, it by no means settles the question. It does not explain emotional glycosuria which so many writers have assumed to be due to a hyperglycemia of more than 170 mg. per hundred cubic centimeters.

Furthermore, there is considerable experimental work which is contrary to Cannon's observations. Thus, Stewart,[9] as a result of work with cats, found that there was no evidence that the degree of excitement of the animals influenced the sugar content of the blood. He did not find a change in the blood sugar following the removal of the suprarenal glands. The average sugar content of the blood for quiet animals was approximately the same as for excited animals of the same group. Stewart does not report the urinary observations in these cases. In another series of experiments on a large group of cats and dogs, Stewart [10] stated "that no significant difference has been found in the blood sugar content of normal animals collected first when they were quiet and again after they had been excited for a time." Stewart doubted whether there is such a thing as emotional hyperglycemia. A number of articles are in opposition to Cannon's theories and give experiments and conclusions contradicting those of Cannon.

Ross and McGuigon,[11] experimenting on animals in connection with the administration of anesthetics, did not find initial hyperglycemia and came to the conclusion that it is the ether more than the excitement that causes the hyperglycemia.

MacLeod [12] repeated the work of Folin and Cannon on medical students and was not able to find glycosuria after the examinations, in spite of the fact that they were made "extremely nerve-racking."

As against the emotional origin of diabetes is the fact that in both Russia and Germany reports have been made of a decrease in the incidence of diabetes in the general population in spite of the tremendous strain of the recent World War.

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9. Stewart, G. N.: Morphine, Hyperglycemia and the Adrenals, Am. J. Physiol. **62**:93, 1922.

10. Stewart, G. N.: Adrenalectomy and the Relation of the Adrenal Bodies and Metabolism, Physiol. Rev. **4**:161, 1924.

11. Ross, Ellison L., and McGuigon, Hugh: The Dextrose and Diastase Content of the Blood as Affected by Ether Anesthesia of Animals Fed on Different Diets, J. Biol. Chem. **22**:407, 1915.

12. MacLeod, J. J. R.: Physiology and Biochemistry in Modern Medicine, footnote in the chapter on carbohydrate metabolism, St. Louis, C. V. Mosby Company, 1922.

Joslin [13] reported: "Soldiers returning from the front did not show sugar in the urine. About 40,000 passed through Mesves, France, where I was consultant; yet, though urines were systematically examined but two cases of diabetes were discovered or at least came to my attention."

In a series of experiments with animals in which they were subjected for many days to constant emotional irritation, Allen [14] was never able to get more than a temporary glycosuria and came to the conclusion that there is no evidence of the nervous or emotional origin of diabetes.

It is apparent that contradictory results have been obtained by these workers and that although Cannon's view of an emotional hyperglycemia followed by glycosuria has been widely accepted, there is considerable evidence against it. All the work quoted so far has been on animals or normal persons.

Considerable work has been done on persons with mental disease. Folin, Dennis and Smillie [3] examined the urine of 192 persons with mental disease. A positive sugar reaction was found in 22. The great majority but not all of the patients who had sugar in the urine suffered from depression, apprehension or excitement.

Kooy [15] quoted Cannon's view of emotional hyperglycemia and reported a number of cases of mental disorder. The vast majority of his patients had a normal amount of blood sugar, but a number showed a definite increase. Kooy thought that there was a marked tendency toward an increased amount of blood sugar in persons with mental disease, particularly in those with melancholia. In the nineteen cases of melancholia which he reported, the blood sugar ranged from 93 to 133 mg., only four patients having a blood sugar above 120 mg.

Uyematsu and Soda [16] examined thirty-two patients with catatonic dementia praecox and found the blood sugar to vary from 77 to 142 mg. and to average 99 mg. As the average for their controls was only 82 mg., they concluded: "The amount is noticeably increased when compared with the normal."

Wuth [17] examined ninety-five patients with mental disease and reported an increase in the blood sugar content in forty-three. His highest average was in those with melancholia, thirty of whom gave an average of 115 mg. of sugar in the serum. On the other hand, Weston reported the blood sugar as normal in thirty persons with mental disease.

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13. Joslin, E. P.: The Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1925, p. 147.

14. Allen, F. M.: Glycosuria and Diabetes, Cambridge, Harvard University Press, 1913.

15. Kooy, K. H.: Hyperglycemia in Mental Disorders, Brain **42**:214, 1920.

16. Uyematsu, S., and Soda, T.: J. Nerv. & Ment. Dis. **53**:5, 1921.

17. Wuth: Der Blutzucker bei Psychosen, Ztschr. f. Psychol. u. Neurol. **64**: 83, 1921.

Raphael and Parsons,[18] after examining a large number of patients with mental disease, reported that, "The fasting levels are well within the normal range and that they, in themselves, carry little diagnostic value."

One of us [19] reported the blood sugar in 229 patients admitted consecutively to Bloomingdale Hospital. An increase in the sugar content of the blood was not found except in cases of paresis and psychosis due to cardiorenal disease.

Hackebusch [20] studied the sugar content of the blood in a number of psychotic patients before and after the occurrence of induced emotions. The patients had not had food or water for three or four hours preceding the test. Blood was then taken with a Bang pipet, and the sugar was estimated by Hagerdorn's method. The patient was then subjected to some treatment which would produce anger or anxiety—being given an unpleasant telegram, told of the illness of a relative, frightened by a fierce bulldog, or shaken. Included in the group were cases of hysteria, anxiety neuroses, drug addiction, psychopathic personality, syphilitic disease of the brain, manic-depressive psychoses, schizophrenia and encephalitis. All showed a consistent rise of the blood sugar from forty-five to sixty minutes after the production of the unpleasant emotion, except in cases of schizophrenia and encephalitis. Hackebusch believed that this demonstrates a dulling of emotions in schizophrenia and encephalitis. The rise of blood sugar was comparatively slight in all cases, varying from 0.002 to 0.018 per cent. It is to be noted that in fifteen cases of schizophrenia studied there was no elevation of the second blood sugar, yet two patients were said to show definite signs of emotional irritation. One convalescent patient with schizophrenia showed an elevation of blood sugar of 0.023 per cent when fed by tube and shaken. The author thought that the increase in blood sugar is always due to the emotional state of the patient.

The results of these studies leave one in possession of a vast amount of contradictory material. How may all this be evaluated and what conclusions, if any, may be drawn from it?

The question of the renal threshold may be raised in this connection. It is commonly assumed that, when the concentration of sugar in the blood is greater than from 170 to 180 mg. per hundred cubic centimeters of blood, dextrose passes through into the urine. Yet it has been shown that the renal threshold may vary under a great many conditions,

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18. Raphael, T., and Parsons, J. P.: Blood Sugar Studies in Dementia Praecox and Manic-Depressive Insanity, Arch. Neurol. & Psychiat. **5**:687 (June) 1921.

19. Bowman, Karl M.: Blood Chemistry in Mental Diseases, Am. J. Psychiat. **2**:379, 1923.

20. Hackebusch, W. M.: Eine objective Untersuchungsmethode der Emotionen in der psychiatrischer Klinik, Ztschr. f. d. ges. Neurol. u. Psychiat. **105**:642, 1926.

some of which are not well understood. Feinblott [7] reported the case of a patient with a blood sugar of 500 mg. without glycosuria. He stated: "A study of relation between hyperglycemia and glycosuria served to emphasize the fact that the renal blood sugar threshold varies in different individuals and in some individuals under different circumstances."

Faber [21] claimed that in some normal persons there is a lowering of the threshold value or an abnormal rise in the blood sugar after the ingestion of a meal, without evidence of diabetes. He held that such a glycosuria is absolutely benign and means nothing. From 20 to 30 per cent of his patients who were not diabetic showed alimentary glycosuria after drinking sweet soup. He concluded that there is a physiologic variation in the threshold in the same person from time to time and that pregnancy and lactation alter this threshold.

Kawashima [22] reported that administration of thyroidin generally causes a rise in the sugar excretion threshold. This rise increases with the prolongation of the treatment.

It would seem possible, therefore, that extreme emotion might alter the renal threshold tolerance for dextrose and that glycosuria would not necessarily be an indication of hyperglycemia. The fact that Cannon reported many cases of glycosuria but no blood sugar content higher than 127 mg. as a result of emotional states would be further argument in favor of this idea.

The case of emotional hyperglycemia reported by Folin and Berglund [4] merits careful consideration. Must this high blood sugar have been caused by emotion or could other causes have produced it? It is well known that asphyxia produces hyperglycemia, Cannon and Bulatao [23] stating that "ether and asphyxia can cause liberation of sugar into the blood by affecting the liver cells directly." Both Stewart and Rogoff [24] and Henderson and Underhill [25] agreed that hyperglycemia occurs when there is deficient oxidation of the blood. Might this be considered as a possible basis for the hyperglycemia in Folin and Berglund's case? There is only one case of this nature cited.

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21. Faber, K.: Benign Glycosuria due to Disturbances in the Blood Sugar Regulating Mechanism, J. Clin. Investigation **3**:203, 1926.

22. Kawashima, S.: The Effect of Thyroid Gland Preparation on the Sugar Excretion Threshold, J. Biochem. **7**:361, 1927.

23. Cannon, W. B., and Bulatao E.: Studies on the Conditions of Activity in Endocrine Glands: XVI. The Rôle of the Adrenal Medulla in Pseudaffective Hyperglycemia, Am. J. Physiol. **62**:295 (April) 1925.

24. Stewart, G. N., and Rogoff, J. M.: The Relations of the Adrenals to Piqure, Hyperglycemia and to the Glycogen Content of the Liver, Am. J. Physiol. **46**:90, 1918.

25. Henderson, Y., and Underhill, F.: Acapnia and Glycosuria, Am. J. Physiol. **28**:275, 1911.

The following case with diametrically opposite manifestations would seem to leave the question unsettled.

A man, who was nonpsychotic, objected to having blood taken for examination for sugar, stating that he felt apprehensive, that he knew he would faint away and that he could not stand having it done. When an effort was made to take the blood, he collapsed on the floor in a faint. Blood was then taken, and the sugar content of the blood was found to be 95 mg. per hundred cubic centimeters of blood.

The two following cases also appear to contradict the theories of emotional hyperglycemia and glycosuria:

J. B., a girl, aged 16, had a severe tantrum. She was angry, excited, overactive and overtalkative. The blood sugar content, estimated before breakfast, after a twelve-hour fast and in the middle of the tantrum, was 64 mg. One month later, when she was in a normal mood, the blood sugar after fasting was 99 mg. Three weeks later, when she was in a normal mood, it was 84 mg.

M. F., a divorcée, aged 42, killed her lover. In a clouded and confused state, she walked to the police station and announced the fact. She became so excited that it required four policemen to hold her. She was brought to the Psychopathic Hospital late in the afternoon. She was depressed and cried and moaned. The urine did not show any sugar. The blood sugar, taken twenty-four hours later, when she was still depressed and crying, was 89 mg.

These cases are cited to show the difficulty of drawing conclusions with regard to this subject.

Maranon's reports on aviators show that a large number of high blood sugar contents were obtained. Although the subjects in cases 9 and 10 were old pilots who went up in their aeroplanes every day and were used by Maranon as controls, it is interesting to note that the blood pressures were abnormally high and that the pulse rates were the highest of the whole series in the examinations made before flight. On the basis of his article it is difficult to see how his controls do anything but confuse the issue. There is likewise no statement as to the length of time since food had been taken. The possibility of alimentary hyperglycemia needs to be considered. His observations are extremely suggestive but can hardly be taken as settling the question.

The work done in mental cases is equally inconclusive. There is, furthermore, the added factor of various physical conditions which might affect the blood pressure independently of any emotional condition.

The sugar content of the blood is modified by many factors. After the ingestion of carbohydrates, there is an increase. This increase ordinarily reaches its maximum in forty minutes but returns to normal in less than two hours, unless a large amount of carbohydrate is taken. There is usually a compensatory decrease below the initial fasting level, as Folin has shown, since the mechanism for storing up sugar continues

for a short time after the blood sugar has returned to normal. This normal curve is affected by various conditions such as the rate of absorption from the gastro-intestinal tract, exercise, emotion, fever and endocrine disorders. Hyperglycemia is also produced by acapnia (Henderson and Underhill [25]), ether anesthesia (Ross and McGuigon,[11] Stewart and Rogoff,[24] Aub and Wu [26]), asphyxia and ether—"ether and asphyxia can cause liberation of sugar into the blood by affecting the liver cells directly"—(Cannon and Bulatao [23]), piqûre, traumatic shock (Aub and Wu [26]), nephritis (Myers [27]), infections (Myers [27]) hyperendocrine functions except that of the pancreas (Myers [27]) and diabetes. There is also evidence that severe physical exertion may affect the sugar content.

Levine and his co-workers [28] examined the blood of eleven participants in the Boston Marathon race. The distance covered was 26 miles and 385 yards. The blood sugar before the race varied from 80 to 110 mg. per hundred cubic centimeters. Following the race, six runners showed an unusually low blood sugar level which varied between 40 and 70 mg. per hundred cubic centimeters. Three men had blood sugar values within the limits of normal variation, and two runners had high blood sugar values. The two latter runners had eaten during the race and shortly before the blood had been taken, which probably accounted for the hyperglycemia. A hyperglycemia seems, therefore, to be the most common change in the blood sugar which one encounters after prolonged exercise. It is also to be remembered that these runners were under a definite emotional strain so that in this respect they might well be compared to some of our overactive and emotionally disturbed patients.

PERSONAL STUDIES

In an effort to settle some of the points in this controversy, we decided to make a study of the sugar content of the blood in patients at the Boston Psychopathic Hospital who showed marked emotional states. The following technic was used:

Blood was taken from patients showing marked emotion of any sort. Blood was taken before breakfast so that there had always been a fourteen-hour fast. The condition of the patient was noted carefully at the time the blood was being taken. The sugar content was determined, the method of Folin and Wu being used. The data obtained were written on cards and then transferred to the

26. Aub, J. C., and Wu, H.: Studies in Experimental Traumatic Shock: III. Chemical Changes in the Blood, Am. J. Physiol. **14**:416 (Dec.) 1920.

27. Myers, V. G.: Chemical Changes in the Blood and Their Chemical Significance, Physiol. Rev. **4**:274, 1924.

28. Levine, Samuel A.; Gordon, Burgess; and Derrick, Clifford L.: Some Chemical Constituents of the Blood Following a Marathon Race, J. A. M. A. **82**:1778 (May 31) 1924.

BLOOD SUGAR IN EMOTIONAL STATES CODE

(December 1, 1926)

(1, 2, 3, 4) Case Number.....

(5, 6) Diagnosis:

(00) D. P.
(01) M. D. M.
(02) M. D. D.
(03) M. D. mixed
(04) M. D. hyp.
(05) Inv. mel.
(06) G. P.
(07) Traum.
(08) Par.
(09) Epil.
(10) Sen.
(11) P. W. P. P.
(12) P. W. men. def.
(13) Undiag. psy.

Psy. w. O. S. D.

(14) Del. inf. dis. Tbc.
(15) Del. inf. dis. Puerp.
(16) Del. unk. or.
(17) C. Ren.
(18) Post Op.

Psy. w. O. B. N. D.

(19) Type und.
(20) Enc. leth.

Alc. Psy.

(21) Path. int.
(22) Ac. hall.
(23) Man. ex.

Psych. N.

(24) Psy.
(25) Neur.

W. out P.

(26) P. P.
(27) M. def.
(28) Epil.
(29) Con. dis.

(ΔΔ) Unk.

(7, 8) Age:..... (ΔΔ unk.)

(9) Sex: (0) Male (1) Female

(10) Physical: (0) Neg. (1) Def. neur. (2) Fever (3) Neph. (4) Infect. (5) Glyco. (6) Vague sym. (7) Others (def.) (Δ) Unk.

(11) Co-operation: (0) Norm. (1) — (2) —— (3) ——— (Δ) Unk.

(12) Activity: (0) Norm. (1) + (2) ++ (3) +++ (4) — (5) —— (6) ——— (Δ) Unk

(13) Talk: (0) Norm. (1) + (2) ++ (3) +++ (4) — (5) —— (6) ——— (Δ) Unk

(14, 15) Mood:

Norm. (00)

Anxiety (07) +, (08) ++, (09) +++

Excitement (16) +, (17) ++, (18) +++

Irritability (25) +, (26) ++, (27) +++

(ΔΔ) Unk.

Agitation (01) +, (02) ++, (03) +++

Depression (10) +, (11) ++, (12) +++

Fear (19) +, (20) ++, (21) +++

Stupor (28) +, (29) ++, (30) +++

Anger (04) +, (05) ++, (06) +++

Elation (13) +, (14) ++, (15) +++

Indifference (22) +, (23) ++, (24) +++

Tension (31) +, (32) ++, (33) +++

(16) Intellect: (0) Clear (1) Clouded (Δ) Unk.

(17) Duration of Acute Symptoms: (0) Less than 1 d. (1) 1-3 d. (2) (4-7 d.) (3) (8-31 d.) (4) (1-11 mos.) (5) (1 yr. +) (Δ) Unk.

(18) No. of this Record..... (Δ) Unk.

(19, 20) No. days elapsed between first and sec. exam..... (ΔΔ Unk.)

(21, 22) No. days elapsed between sec. and third exam..... (ΔΔ Unk.)

(23, 24, 25) Blood Sugar..... (ΔΔΔ Unk.)

printed code sheets by underlining the proper item under each heading. A sample code sheet is shown. From these code sheets a standard punch card, used for mechanically sorting and tabulating frequency, distribution and association tables, was made.

MATERIAL

One hundred and forty-eight patients showing emotional states of various kinds were studied at the Boston Psychopathic Hospital. As a second group, 147 examples were taken from a group of cases studied at Bloomingdale Hospital and reported in the *American Journal of Psychiatry*.[19] It was thought that this second group afforded an excellent check on the first. In order to make patients from Bloomingdale Hospital

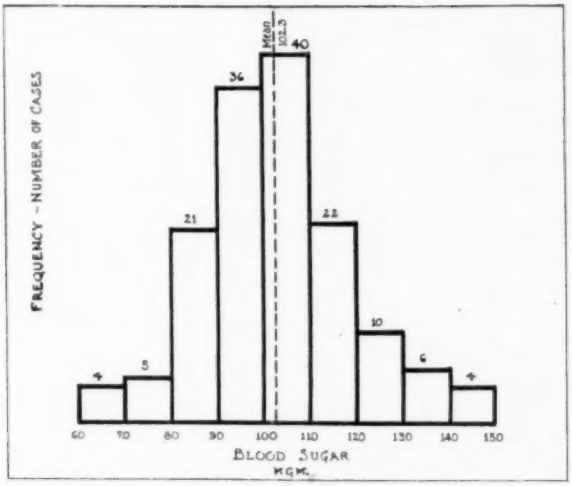

Chart 1.—Distribution of 148 readings of blood sugar values from the Boston Psychopathic Hospital.

comparable with those from the Boston Psychopathic Hospital, only nondiabetic patients and those who had fasted for twelve hours were included.

Chart 1 shows the distribution of the cases from the Psychopathic Hospital and chart 2 that of the curve of the combined cases from the Boston Psychopathic Hospital and the Bloomingdale Hospital. It will be seen that the two curves are similar and the mean is 102.3 for the cases from the Boston Psychopathic Hospital and 103.8 for the combined groups.

Four tables were made showing the distribution according to sex. These distributions are essentially normal (with the exception of the females from the Boston Psychopathic Hospital, who show a slightly higher rating in groups 110 to 150 than would be expected in a chance distribution). The four samples do not differ significantly in distribu-

tion, as shown by the standard deviation of the standard deviation allowing two times the standard deviation from the mean for "scatter." We find that two thirds of the readings fall within these limits. The conclusion from this is that sex does not play a significant rôle in the determination of the blood sugar.

As controls, forty-one cases of normal persons, mostly members of the staff of the Boston Psychopathic Hospital, are given in table 4. It will be seen from this that the control cases show a considerably lower blood sugar than do the psychotic cases. The mean is 91 and the highest blood sugar is 116. The question therefore arises as to what should be regarded as a normal blood sugar.

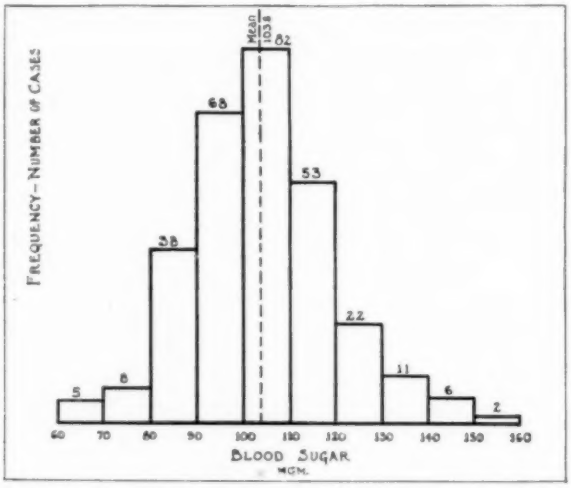

Chart 2.—Distribution of 295 readings of blood sugar values from the Boston Psychopathic and the Bloomingdale Hospitals.

Table 5 gives the distribution curve of the fasting blood sugar in 431 persons who were clinically normal. According to Gray [29] "the average is 0.09 per cent and the most frequent value 0.10 per cent, the minimum 0.04 per cent, the maximum 0.16 per cent." Gray secured these results from a number of sources and did not give any data as to the number or size of the samples used. If this table of Gray's were used as a standard for comparison, the blood sugar values of patients from the Psychopathic Hospital would be considered normal.

Recently, John [30] published the results of a study of 22,808 blood sugar estimations in nondiabetic persons. He expressed the belief that

29. Gray, Horace: Blood Sugar Standards, Arch. Int. Med. **31**:241 (Feb.) 1923.

30. John, H. J.: A Study of 22,808 Blood Sugar Estimations—Fasting and Postprandial—in Non-Diabetic Individuals, Ann. Int. Med. **1**:470 (Jan.) 1928.

TABLE 2.—*One Hundred and Forty-Eight Blood Sugar Readings According to Sex, Boston Psychopathic Hospital, 1924-1925*

Blood Sugar, Mg.	Male	Female	Total
60- 69	0	4	4
70- 79	2	3	5
80- 89	4	17	21
90- 99	10	26	36
100-109	18	22	40
110-119	4	18	22
120-129	1	9	10
130-139	0	6	6
140-149	0	4	4
Total	39	109	148
Mean, M	99.7 ± 1.8	103.2 ± 1.7	102.3 ± 1.4
Standard deviation	10.9 ± 1.2	17.7 ± 1.2	16.6 ± 0.9

TABLE 3.—*Blood Sugar Readings According to Sex, Bloomingdale Hospital, 1919-1920*

Blood Sugar, Mg.	Male	Female	Total
60- 69	1	0	1
70- 79	3	0	3
80- 89	7	10	17
90- 99	17	15	32
100-109	19	23	42
110-119	18	13	31
120-129	6	6	12
130-139	3	2	5
140-149	0	2	2
150-159	1	1	2
Total	75	72	147
Mean, M	104.5 ± 1.7	105.0 ± 1.8	104.7 ± 1.3
Standard deviation	15.1 ± 1.2	15.3 ± 1.3	15.2 ± 0.9

TABLE 4.—*Forty-One Blood Sugar Readings of Clinically Normal Persons, Staff of Boston Psychopathic Hospital*

Blood Sugar, Mg.	Male	Female	Total
Under 70	0	0	0
70- 79	1	3	4
80- 89	9	6	15
90- 99	11	7	18
100-109	1	2	3
110-119	1	0	1
120 and over	0	0	0
Total	23	18	41
Mean, M	92.8 ± 1.5	88.7 ± 2.0	91.0 ± 1.2
Standard deviation	7.3 ± 1.1	8.4 ± 1.4	7.5 ± 0.8

TABLE 5.—*Blood Sugar During Fasting in Four Hundred and Thirty-One Persons Clinically Normal*

Blood sugar	0.04	0.05	0.06	0.07	0.08	0.09	0.10	0.11	0.12	0.13	0.14	0.15	0.16
Number	2	6	22	34	59	97	116	66	19	8	0	1	1

the blood sugar increases with age and gave a chart showing the average blood sugar content for each decade based on blood sugar values in 1,000 nondiabetic fasting persons. During the first decade the average blood sugar content is 91.8 mg.; the average for the second decade is 94 mg.; for the third, 96.4 mg.; for the fourth, 98 mg.; for the fifth, 100.9 mg.; for the sixth, 101 mg.; for the seventh, 102.7 mg.; for the eighth, 107.4 mg.

John found that in 6,475 fasting persons the blood sugar content in 14.73 per cent was 80 mg. per hundred cubic centimeters or less, and

TABLE 6.—*Blood Sugar and Diagnosis in One Hundred and Forty-Eight Cases of Psychosis, Boston Psychopathic Hospital*

	Blood Sugar, Mg.									
	60-69	70-79	80-89	90-99	100-109	110-119	120-129	130-149	Total	Mean, M.
Dementia praecox	0	1	4	3	4	2	2	0	16	98.9
Manic-depressive psychoses										
Manic	0	1	3	8	9	5	1	3	30	104.5
Depressive	1	0	6	11	6	5	2	3	34	102.1
Hypomanic	0	0	0	2	0	1	0	0	3	98.0
Mixed	1	0	2	0	1	1	1	0	6	98.3
Involutional melancholia	0	0	1	1	0	1	1	0	4	106.2
General paresis	0	0	0	1	4	3	1	0	9	109.1
Traumatic psychoses	0	1	0	1	0	0	0	0	2	85.5
Senile psychoses	0	0	0	0	1	0	0	1	1	117.0
Epileptic psychoses	0	0	0	1	0	0	0	0	1	93.0
Paranoid condition	0	0	0	0	1	0	0	0	1	109.0
Psychoses with psychopathic personality	1	0	0	1	0	0	0	0	2	81.0
Psychoses with mental deficiency	0	0	1	0	1	0	0	0	2	94.5
Undiagnosed psychoses	0	1	1	2	7	1	1	1	14	103.4
Psychoses with other somatic diseases	0	0	1	3	3	1	0	1	9	103.0
Psychoses with other brain and nervous diseases										
Type undetermined	0	0	0	0	1	0	1	0	2	114.0
Epidemic encephalitis	0	0	2	0	1	0	0	1	4	105.3
Alcoholic psychoses	1	0	0	0	2	0	0	1	4	105.8
Psychoneuroses	0	1	0	2	0	1	0	0	4	93.5
Total psychoses	4	5	21	36	40	22	10	10	148	102.8

was as low as 30 mg. per hundred cubic centimeters in some cases. As he arbitrarily discarded all blood sugar readings of more than 120 mg., he did not provide data on the occurrence of so-called high blood sugar values. However, 31 per cent of the blood sugar values during the fasting are between 100 and 120 mg., 27 per cent between 90 and 100 mg., and 26 per cent between 80 and 90 mg.

Table 6 gives the distribution of the blood sugar according to diagnoses. The distribution is essentially normal and does not show any particular tendency in any one disease toward a high blood sugar content.

Table 7 shows the correlation between the physical manifestations and the blood sugar. There are more cases showing positive physical

manifestations than one would expect by chance alone in the groups showing high blood sugar values. The distribution is otherwise normal.

Table 8 shows the distribution of positive physical manifestations. There are more cases showing fever and vague symptoms than one would expect by chance alone in the groups showing high blood sugar values. The distribution is otherwise normal.

Table 9 gives the correlation between the activity and the blood sugar. Separate distributions for males and females show an essentially normal correlation.

TABLE 7.—*Blood Sugar and Physical Signs in One Hundred and Forty-Eight Cases, Boston Psychopathic Hospital*

Blood Sugar, Mg.	Number of Cases with Physical Signs			
	Positive	Negative	Not Stated	Total
60- 69	1	1	2	4
70- 79	3	2	0	5
80- 89	13	8	0	21
90- 99	24	11	1	36
100-109	30	8	2	40
110-119	14	7	1	22
120-129	6	3	1	10
130-139	6	0	0	6
140-149	4	0	0	4
Total	101	40	7	148

TABLE 8.—*Distribution of Positive Physical Signs in One Hundred and One Cases, Boston Psychopathic Hospital*

Blood Sugar, Mg.	Definite Neurologic Signs	Fever	Nephritis	Infection	Glycosuria	Vague Symptoms	Others (Definite)	Overweight	Underweight	Total No. of Signs
60- 69	0	0	0	0	0	1	0	0	0	1
70- 79	1	0	0	0	1	0	1	0	0	3
80- 89	1	3	1	0	0	4	4	2	1	16
90- 99	2	2	1	0	1	10	7	2	3	28
100-109	6	2	0	0	1	11	13	3	3	39
110-119	1	1	0	0	0	5	5	4	2	18
120-129	0	3	0	0	0	4	0	2	1	10
130-139	0	4	0	0	0	0	3	1	0	8
140-149	0	0	0	0	0	4	0	0	0	4
Total	11	15	2	0	3	39	33	14	10	127

Tables 10 and 11 show the correlation between the moods and the blood sugar. If we eliminate those with normal mood at the time the blood sugar value was taken, there are ninety-nine females and thirty-eight males showing some abnormal mood or moods. The females show a greater range of moods. Anger, anxiety, fear and stupor do not appear among the males. There are also more moods per capita among females than males. The most frequent combinations among females are agitation and depression (twenty-two cases) and excitement and elation (thirteen cases). The only suggestion of association of high blood sugar content and mood occurs in nine females with blood sugar values of 120 and over who displayed excitement. Moods were also sorted

according to their intensity, 1+, 2+, 3+ (tables not printed). Only four very intense (3+) moods appear among males and forty-one among females. Of the nine cases in females with associated high blood sugar values and excitement, seven showed the 3+ mood.

Distributions were also made to a test for association between blood sugar and (1) agitation, (2) agitation and depression and (3) agitation and excitement. Distributions were essentially normal in each case.

TABLE 9.—*Blood Sugar and Activity in One Hundred and Forty-Eight Cases, Boston Psychopathic Hospital*

Blood Sugar, Mg.	Activity								
	— — —	— —	—	Normal	+	++	+++	Unknown	Total
60- 69	0	0	1	3	0	0	0	0	4
70- 79	0	0	0	2	1	1	1	0	5
80- 89	0	3	2	6	4	4	2	0	21
90- 99	2	1	2	11	8	7	5	0	36
100-109	0	0	5	10	10	7	7	1	40
110-119	0	0	1	5	5	7	4	0	22
120-129	0	1	2	1	2	0	4	0	10
130-139	0	1	0	0	2	2	1	0	6
140-149	0	0	0	1	1	0	2	0	4
Total	2	6	13	39	33	28	26	1	148

TABLE 10.—*Blood Sugar and Moods in One Hundred and Nine Female Patients, Boston Psychopathic Hospital*

Blood Sugar, Mg.	Number of Patients	Mood												Total Number of Entries
										Others				
		Normal	Agitation	Depression	Elation	Excitement	Indifference	Irritability	Tension	Anger	Anxiety	Fear	Stupor	
60- 69	4	1	1	0	1	0	0	1	1	0	0	0	0	5
70- 79	3	0	1	1	0	1	0	1	0	0	1	0	0	5
80- 89	17	2	4	8	1	3	1	0	4	0	0	1	1	25
90- 99	26	1	6	12	10	8	0	0	3	0	1	2	1	44
100-109	22	4	6	8	3	10	0	0	1	0	0	3	0	35
110-119	18	2	6	8	3	7	0	0	2	1	1	1	0	31
120-129	9	0	3	4	1	4	0	0	1	0	0	1	0	14
130-139	6	0	2	2	0	2	0	0	1	0	0	0	0	7
140-149	4	0	0	1	0	3	0	0	0	0	0	0	0	4
Total	109	10	29	44	19	38	1	2	13	1	3	8	2	170

Distributions for blood sugar and cooperation, talk, intellect and duration of acute symptoms are normal and are not printed.

If one takes the commonly accepted standards for normal amounts of blood sugar, then only in those patients whose blood sugar value is more than 120 mg. would it be regarded as abnormally high. A study of these cases shows that there are nine with a blood sugar between 120 and 129; six between 130 and 139 and 4 between 140 and 149. The nine cases in which the content was between 120 and 129 may be summarized as follows:

CASES SHOWING A HIGH SUGAR CONTENT

CASE 1.—A woman, aged 30, with a condition diagnosed as manic-depressive depression, was 80 pounds (36.3 Kg.) underweight, quite underactive and markedly depressed, the depression having lasted for two weeks. The blood sugar was 120 mg.

CASE 2.—A woman, aged 22, with a psychosis diagnosed as dementia praecox, showed a blood sugar of 120 mg. It was considered possible that this patient had not fasted for twelve hours so a second blood sample was taken; the sugar content was 89 mg. The mental condition was the same at both times.

CASE 3.—A woman, aged 50, with a psychosis diagnosed as dementia praecox, had a blood nonprotein nitrogen of 60; the urine contained hyaline casts, and there had been fever preceding this period. The patient was markedly excited, overactive and intellectually was clouded. The blood sugar was 120 mg.

CASE 4.—A woman, aged 43, with a psychosis diagnosed as involutional melancholia, had developed malaria seven months previously; the depression had started

TABLE 11.—*Blood Sugar and Moods in Thirty-Nine Male Patients, Boston Psychopathic Hospital*

Blood Sugar, Mg.	Number of Patients	Mood									Total Number of Items
		Normal	Agitation	Depression	Elation	Excitement	Indifference	Irritability	Tension	Others	
60- 69	0	0	0	0	0	0	0	0	0	0	0
70- 79	2	0	0	0	0	2	0	0	0	0	2
80- 89	4	0	2	3	0	0	1	0	2	0	8
90- 99	10	1	1	2	1	4	1	1	1	0	12
100-109	18	0	2	4	6	5	2	1	2	0	22
110-119	4	0	0	0	2	3	0	0	0	0	5
120-129	1	0	0	0	0	1	0	0	0	0	1
130 and over	0	0	0	0	0	0	0	0	0	0	0
Total	39	1	5	9	9	15	4	2	5	0	50

with delirium and malaria at this time. She was markedly depressed and agitated, but her intellect was clear. The blood sugar was 121 mg.

CASE 5.—A woman, aged 37, with a psychosis diagnosed as manic-depressive of mixed form, had a temperature of 100.2 F. at the time the blood was taken. She was markedly overactive, excited, fearful and uncooperative. The blood sugar was 122 mg.

CASE 6.—A woman, aged 32, with a psychosis diagnosed as manic-depressive depression, presented no abnormal physical signs. She was moderately depressed and agitated, and slightly overactive. The blood sugar was 123 mg.

CASE 7.—A woman, aged 49, with a condition diagnosed as paresis, was 5 feet (152.4 cm.) tall and weighed 215 pounds (97.5 Kg.). X-ray examination showed a large sella which was considered abnormal. She was mildly elated and normally active, and the intellectual functions were impaired. The blood sugar was 124 mg.

CASE 8.—A woman, aged 20, with a condition diagnosed as psychosis with other brain or nervous diseases of undetermined type, presented irregular and sluggish pupils; the temperature was 101 F. two days before the sample of blood was taken. She was moderately depressed and somewhat underactive. The blood sugar was 125 mg.

CASE 9.—A woman, aged 50, with a psychosis diagnosed as manic-depressive excitement, had a temperature of 100 F. She was markedly overactive, overtalkative and excited. The blood sugar was 128 mg.

In six cases the blood sugar was between 130 and 139 mg.

CASE 10.—A woman, aged 45, with a psychosis diagnosed as manic-depressive excitement, had a temperature of 101 F. and was markedly overactive, overtalkative and excited. The blood sugar was 133 mg. A week later the patient showed the same mental and physical symptoms. The blood sugar was 137 mg. and the nonprotein nitrogen was 65. Two weeks later, with a temperature of 102.2 F. and with the same mental symptoms, the blood sugar was 187 mg.

CASE 11.—A woman, aged 35, with a psychosis diagnosed as manic-depressive excitement, a temperature of 100 F., was moderately overactive, overtalkative and excited. The blood sugar was 133 mg. Four days later, the temperature was normal, the mental symptoms were unchanged except that she was a little less active and the blood sugar was 122 mg.

CASE 12.—A woman, aged 32, with a condition diagnosed as a psychosis with somatic disease of cardiorenal type, had aortic insufficiency and was 25 pounds (11.3 Kg.) overweight. The temperature was 101.2 F., the white blood cell count was 14,600 and the urine showed a slight trace of albumin. She was moderately overactive, overtalkative and agitated and was in a delirious condition. The blood sugar was 136 mg.

CASE 13.—A woman, aged 38, with a psychosis diagnosed as manic-depressive depression, also had pulmonary tuberculosis. She was markedly depressed and agitated, and intellectually was slightly clouded. The blood sugar was 138 mg.

CASE 14.—A woman, aged 60, with a psychosis diagnosed as manic-depressive depression, had sustained a fractured spine and foot as a result of a suicidal attempt three days before the blood was taken. She was moderately depressed and tense. The blood sugar was 132 mg. Two weeks later, the mental symptoms were unchanged; the blood sugar was 112. Two days after this, with mental symptoms unchanged, the blood sugar was 100 mg.

CASE 15.—A woman, aged 35, with a psychosis that was not classified, had a temperature of 100.4 F. with a white blood cell count of 14,700. She was moderately excited and was clouded intellectually. The blood sugar was 131 mg.

Four cases showed blood sugar above 140 mg.

CASE 16.—A woman, aged 42, with a psychosis diagnosed as acute alcoholic hallucinosis, showed general weakness, wasting of limbs, tremor and hyaline casts in the urine. She was markedly excited and overactive and was clouded intellectually. The blood sugar was 140 mg.

CASE 17.—A woman, aged 39, with a psychosis diagnosed as manic-depressive depression, had just weaned an infant and had galactose in the urine. The pupils were sluggish. She had fallen downstairs a week before admission. She was slightly depressed. The blood sugar was 143 mg.

CASE 18.—A woman, aged 17, with a condition diagnosed as epidemic encephalitis, was markedly excited and overactive. The blood sugar was 146 mg.

CASE 19.—A woman, aged 42, with a psychosis diagnosed as manic-depressive excitement, had a temperature of 100 F. and a white blood cell count of 26,600. She had bronchopneumonia. She was markedly excited and overtalkative but only slightly overactive. The blood sugar was 149 mg. Ten days later, the mental symptoms were essentially unchanged; she had slight jaundice; the white blood cell count was 21,600; the temperature was normal on this day but on the day

following it was 102.4 F. and the day preceding it had been 100.6. The blood sugar was 148 mg. Five weeks later, the temperature was 99.8 and she had essentially recovered, both physically and mentally. The blood sugar was 88 mg.

Careful study of the cases presenting high blood sugar values shows that physical factors which might easily affect the sugar content of the blood were present in many. It becomes difficult, therefore, to state to what extent the physical factors entered into the production of the high blood sugar content and to what extent emotion might have been the cause.

CASES SHOWING A LOW SUGAR CONTENT

CASE 20.—A man, aged 58, with a condition diagnosed as traumatic psychosis, had injured his head four weeks before examination of the blood. The urine showed +++ sugar three days before the examination of the blood. He had been delirious for three weeks. Mentally, he was moderately active, excited and overtalkative and was clouded intellectually. The blood sugar was 73 mg.

CASE 21.—A youth, aged 18, who had had epileptic attacks all his life, came into the hospital with an unclassified excitement of two days' duration. The pupils were irregular, the deep reflexes unequal, and the urine showed albumin and casts. The white blood cell count was 14,800. X-ray examination showed a thin walled skull, probably due to hydrocephalus. The patient was markedly excited and overactive and was clouded intellectually. The blood sugar was 70 mg.

CASE 22.—A woman, aged 20, with a manic-depressive psychosis of mixed type, presented no abnormal physical signs. She was moderately elated, irritable and overtalkative. The blood sugar was 69 mg.

CASE 23.—A woman, aged 32, with a psychosis diagnosed as manic-depressive depression, was 18 pounds (8.2 Kg.) overweight, and the basal metabolism was —15. She was slightly depressed. The blood sugar was 67 mg. Eight days later, with the mental condition unchanged, the sugar was 76 mg.

CASE 24.—A woman, aged 45, with an alcoholic psychosis of the type of pathologic intoxication, was moderately tense and slightly agitated, with questionable clouding of intellectual functions. The blood sugar was 69 mg.

These cases indicate that a low blood sugar content may occur with extreme emotion and with physical signs similar to those associated with some abnormally high blood sugar values.

SUMMARY

The data reported from outside sources concerning the effect of emotional states on the sugar content of the blood are contradictory. There is considerable evidence that emotional states produce a rise in the sugar content of the blood, but equally good evidence that the sugar content is unaffected. The data with regard to psychotic patients are equally confused and contradictory. A study of 148 cases of mental diseases of various kinds with different types of emotional states show that in the majority of these cases the blood sugar content was normal according to accepted standards of from 80 to 120 mg. of dextrose per

hundred cubic centimeters of blood. The distribution curve was normal and agreed essentially with the curve of 431 persons who were clinically normal which is given by Gray [29] and 6,475 blood sugar values in non-diabetic persons described by John.[30] In our 41 control cases the blood sugar content was considerably lower than in the psychotic cases. A number of these samples of blood, however, were taken immediately after the person was awakened from a night's sleep. It is possible that the blood sugar content is lower then than after the person is up and around.

Analysis of the various factors that might be concerned with the high blood sugar values shows that more cases showing fever and vague physical symptoms presented high blood sugar contents than would be expected as a result of chance alone.

The only association between high blood sugar values and mood occurs in nine women with blood sugars of 120 and over who displayed excitement. Otherwise there was no correlation between mood and high blood sugar content; furthermore, in some cases an abnormally low amount of blood sugar occurred with excitement, depression and other abnormal emotional conditions.

CONCLUSIONS

In persons with mental disease, the blood sugar during fasting is usually within normal limits; there is no correlation between the mood of the patient and the height of the blood sugar; various other factors might account for a great many instances of high blood sugar values. It seems probable that physical conditions, particularly fever, are more concerned with the high blood sugar values found in our study than is the emotional state of the patient.

The following suggestion for further study may be offered. If the blood sugar content is not increased in psychotic patients with abnormal emotional states, this may be due to the following hypotheses: 1. The kidney threshold at which dextrose passes over into the urine might be lowered. This would account for the glycosuria which often results and might serve to keep down the amount of sugar in the blood. 2. Depletion of the glycogen content of the liver might prevent a rise in the amount of blood sugar. The overactivity of the patient together with failure to take sufficient food might produce such a depletion. 3. The emotion of the psychotic patient may be a qualitatively different condition from the emotion of the normal person. It is possible that there might be an absence of any active stimulation to the sympathetic nervous system which, according to Cannon's theory, is necessary for the production of hyperglycemia.

PATHOLOGIC SLEEP AND SIMILAR CONDITIONS

STUDIED BY THE ELECTRICAL SKIN RESISTANCE METHOD *

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Narcolepsy was unknown as a specific pathologic manifestation until 1880, when Gélineau [1] described the process and differentiated it clearly from the similar epileptic condition. Since then, practically all efforts to study the disease by laboratory methods have been unproductive, and there has been no evidence of any symptoms other than cataplexy and extreme somnolence. On the basis of observations of the skin resistance of normal subjects, it appeared that some significant data might be gained from an investigation of pathologic sleeping conditions according to the electrical skin resistance method.

From prolonged studies of normal sleep by this method, a few simple facts have been established. It has been found, for instance, that the skin resistance of the palms of the hands increases roughly in proportion to the depth of the sleep, that the increase seems to depend on changes in the activity of the sweat glands, and that sudden awakening causes an instantaneous decrease to a waking level.[2] The phenomenon is similar to the pupillary changes occurring in the eye, since the pupil contracts during sleep in proportion to the depth of sleep and dilates with awakening to its usual diameter.[3]

The electrical response of the skin on the back of the hand is independent of that on the more porous areas of the palm. The dorsal resistance does not show an invariable constant rise, but seems to increase during a relaxed, quiet sleep, and to decrease during a tense, strained sleep. This theory is borne out by the fact that the dorsal resistance fluctuates with degrees of tenseness in the waking state, decreasing during periods of obvious tension and increasing with marked relaxation and calm. It seems to be independent of the nervous system and controlled largely by local changes in the epithelial cells.

On the basis of these results and those reported from records on many normal subjects and psychopathic patients in the waking state,[4] the patients have been examined in nine cases of narcolepsy in which

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* Submitted for publication, July 13, 1928.

* From the Psychobiological Laboratory, Johns Hopkins University School of Medicine.

1. Gélineau: Gaz. d. hôp. **53**:626, 1880.
2. Richter, C. P.: Proc. Nat. Acad. of Sc. **12**:214, 1926.
3. Brown-Séquard, C. E.: Arch. de physiol. **21**:739, 1889.
4. Richter, C. P.: Electrical Skin Resistance, Arch. Neurol. & Psychiat. **19**:488 (March) 1928.

both somnolence and cataplectic attacks occurred. Five of these cases have been studied extensively, but detailed records will be presented of only two of them in which numerous observations were made over periods of three weeks or more. In addition records will be presented of one patient whose condition was diagnosed as hysterical and who complained of excessive sleep without cataplexy, and of three others whose condition was diagnosed as schizophrenic stupor. These records resemble those of narcoleptic patients and differ greatly from those of other hysteric and schizophrenic patients. It is interesting to note, moreover, that the last three patients appeared somewhat different clinically from other schizophrenic patients.

METHODS

The methods used in the present experiments have been described in detail in previous papers.[5] The electrodes consisted of zinc disks and a paste made by mixing kaolin with saturated zinc sulphate solution. One electrode was attached to the palm and back of each hand in order that the resistance of the palms and backs might be measured separately. This is important because differently constructed areas of the skin are physiologically independent. An imperceptible constant galvanic current was passed through the body, and the resistance was measured with a string galvanometer.

The experiments can be divided into two groups: 1. Readings of the skin resistance were made at the same time daily over the entire period in which the patients remained at the clinic (at least three weeks). 2. Readings were taken during attacks of sleep either spontaneous in origin or produced experimentally by the removal of as many disturbing stimuli as possible. For this purpose the patient was blindfolded and placed in a comfortable chair in a quiet room, at a place where he could be observed at all times without being disturbed. In order that frequent readings might be taken without awakening him, the electrodes were left attached during the entire time he slept.

RESULTS

1. Average Daily Skin Resistance in the Narcoleptic Patients During the Waking State.—From all five of the narcoleptic patients studied, unusual records of the skin resistance were obtained. The average daily palm-palm resistance during their waking intervals was high in every case, but it was highest in the patient who slept the most.[6]

Case 1.—A colored girl, aged 9, began to sleep excessively after receiving a blow on the head and was sleeping from eighteen to twenty hours a day when she came under observation in the hospital. She is known to have collapsed on several occasions while playing with other children, but she did not show any cataplectic tendencies during her stay in the hospital. The chart of her daily resistance, shown in figure 1, may be compared with typical records from a normal person, shown in figure 2. The resistance in ohms is given on the ordinates, and

5. Richter, C. P.: Brain **50**, part 2, 216, 1927.

6. Clinical observations of this patient were made by Weech, A. A.: Am. J. Dis. Child. **32**:672 (Nov.) 1926.

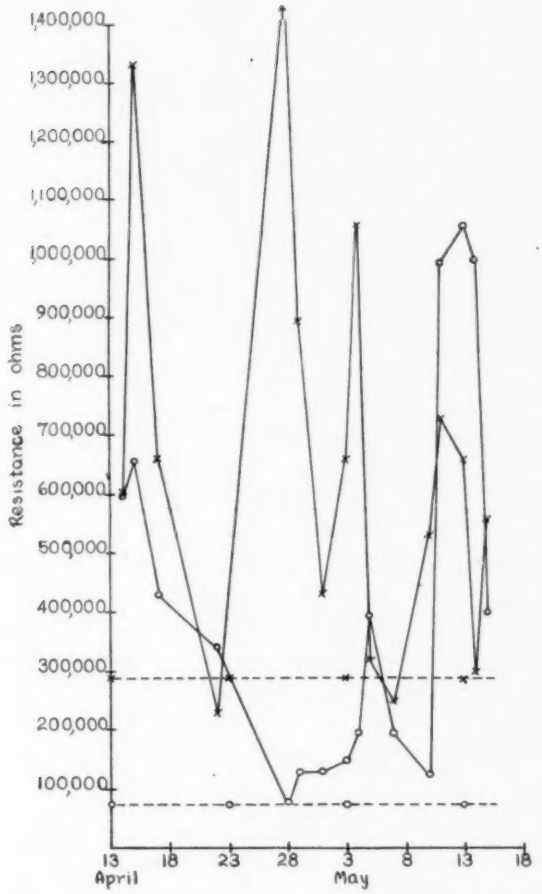

Fig. 1.—Daily skin resistance readings on a narcoleptic girl, aged 9. The resistance in ohms is given on the ordinates and the duration of the experiment in days on the abscissas. The palm-palm readings are presented by the X lines and the back-back readings, by the O lines. The average normal levels are given similarly in dotted lines.

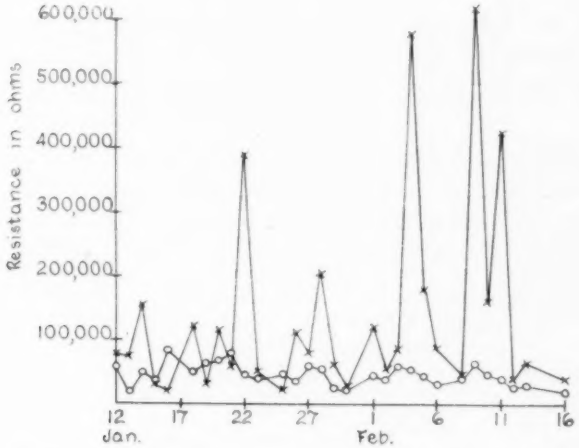

Fig. 2.—Daily skin resistance readings on a normal man. The constancy of the palm-palm curve and the relatively low level maintained in the back-back curve contrast sharply with the record presented in figure 1.

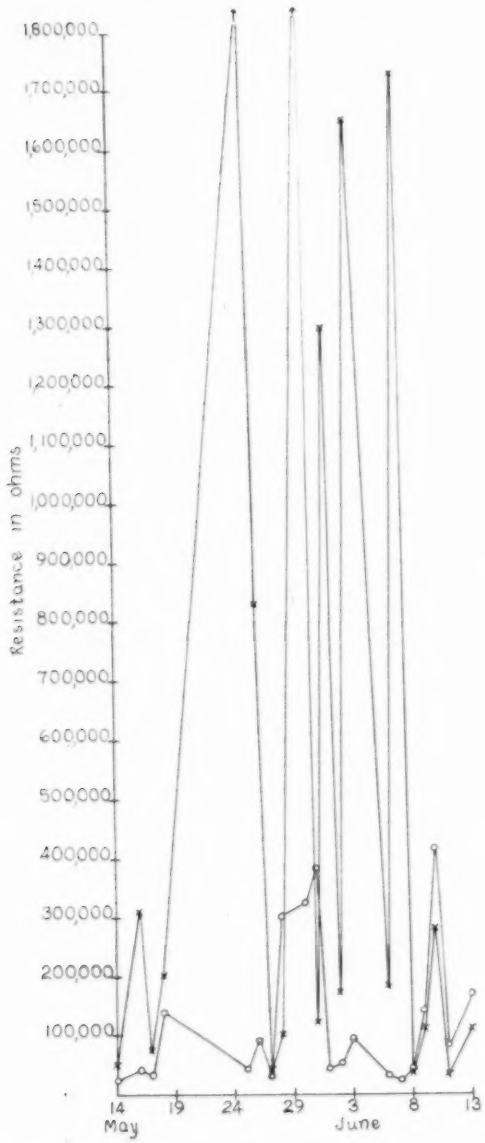

Fig. 3.—Daily skin resistance readings from a narcoleptic girl, aged 16.

the duration of the experiment in days on the abscissas. Records taken each day over a period of several months show that her daily palm-palm resistance was always much higher than that of normal subjects in a waking state, and on many days it was well above the level found in normal persons in a deep sleep. On three days it reached 1,000,000 ohms, and the average for the entire period of observation was 418,450 ohms—350,000 ohms higher than the normal average of 77,100. Her average back-back resistance was also very high—687,000 ohms as compared to the normal average of 290,310. It is important to note that at times when the resistance was high the patient slept almost continuously, although she was able to walk when roused and responded in a drowsy manner when stimulated.

CASE 2.—The daily record of another narcoleptic patient, shown in figure 3, is characterized by a high average resistance on both the palms and backs of the hands, with extreme fluctuations from day to day. The palm-palm readings ranged from 20,000 to 420,000 ohms, the back-back readings from 30,000 to 2,934,000 ohms.

These two records illustrate the chief difference in the daily resistance curves of normal and narcoleptic persons. It was shown in a previous paper that the daily palm-palm resistance of normal subjects is maintained at a low level with few fluctuations. The palm-palm readings of the narcoleptic subjects are of special interest because they are much higher than the normal and vary considerably. Likewise, the daily back-back readings are high and fluctuate more widely than normal. Schizophrenic patients in a catatonic stupor also have a high average back-back resistance with marked variations, but they can be distinguished from the narcoleptic subjects because they show extremely low rather than high palm-palm averages. Thus it may be seen that although the skin resistance occasionally drops to a normal level in narcoleptic persons, its average is considerably higher.

On the basis of the present knowledge of skin resistance and its significance, the records from the narcoleptic patients may be interpreted in the following way: The high palm-palm resistance represents a quantitative change in the direction of sleep even during the waking state. The high back-back resistance with the marked fluctuations indicates a lack of tenseness and an instability of the mechanisms involving muscle tone, which is consistent with the clinical knowledge of the cataplectic attacks.

CASE 3.—The daily galvanometric records of a man who had attacks of sleep but no cataplexy are interesting in this connection. This patient was not narcoleptic and the attacks of sleep, which occurred infrequently, were regarded as a hysterical manifestation, chiefly because they seemed to be precipitated on several occasions when certain details of his marital situation were brought to his attention. His daily resistance chart is shown in figure 4. The palm-palm and back-back resistance are both higher than the normal average and show relatively large fluctuations. It is important to note that early in the investigation the palm-palm resistance began to increase suddenly from a level near 60,000 ohms, and after twenty days of steady rising exceeded 300,000 ohms. When it reached 200,000, the patient had one severe attack of sleep which lasted several hours, and when the highest point was reached a week later, he had the most severe and prolonged

attack of all that occurred during his entire stay in the clinic. These records suggest that the attacks of sleep were on some basis other than simple hysteria, and the history of the case revealed a number of facts consistent with this conception: (1) there was a record of influenza in 1918 with fever for seven days and stupor for four days; (2) it was found that in 1923, a year before admission to the clinic, he began having frequent attacks of sleep, followed by a general weakness, slow gait and speech, diplopia, and amnesia during the duration of the attack. During the period of sleep, which lasted from one to five days, the patient

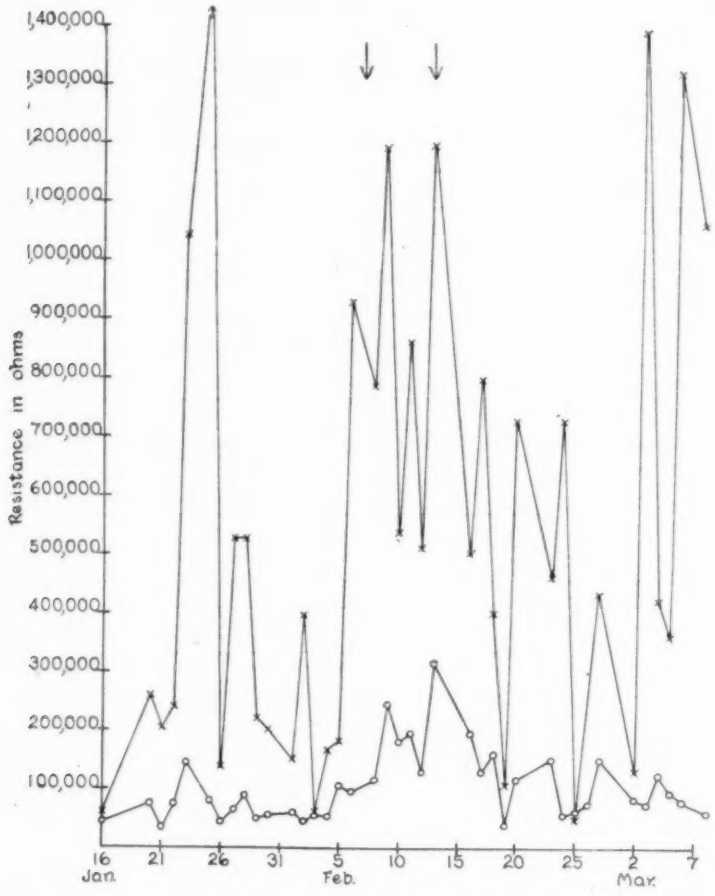

Fig. 4.—Daily skin resistance readings from a patient who suffered from attacks of sleep which were thought to be hysterical in origin. He did not show cataplexy, and his attacks of sleep were relatively infrequent. The attacks which occurred during the period represented on the chart are indicated by large arrows.

awakened just long enough to eat a large meal and then dropped off to sleep again. In view of the clinical and laboratory records, there seemed little doubt that in this patient one was dealing with some disturbance of the sleep mechanism, probably due to an encephalitic process, complicated and exaggerated by the strain of a difficult marital situation.

The records of all the narcoleptic patients present several unusual features which differentiate them clearly from normal records: 1. The skin resistance of the dorsal and palmar surfaces of the hands often increases greatly while the patient is sitting quiet and undisturbed. Under the same conditions normal persons usually show a decrease of both dorsal and palmar resistance. 2. Great fluctuations, especially in palmar resistance, occur from moment to moment. Such variations do not arise in normal persons. The rapid increase in the dorsal resistance, probably indicates a marked tendency in these patients to quick muscular relaxation. A similar increase has been found after relaxation from emotional strain in a few normal persons and in two patients with high blood pressure. It occurs also during a relaxed sleep, but even then the increase is not as rapid as it is in the narcoleptic patients. The large, rapid increase and the marked fluctuations in the palmar resistance seem to indicate, on the other hand, that the sleep mechanism comes into play much more readily in these patients than in normal persons and that it is much less stable. These changes in palmar and dorsal resistance in the narcoleptic patients are of particular interest because they can be detected even when other changes are not apparent to the casual observer.

Such differences in skin resistance are significant only as indirect evidence of some alteration in the vegetative centers in the brain, especially in the region of the third ventricle which controls the sleep reaction. It must be that the injury, of whatever nature, affects not only the sleep mechanism but also the centers which control the action of the sweat glands and produce changes in palmar resistance, and the centers which control muscle tone and produce changes in the dorsal resistance.

2. Changes in Skin Resistance in Narcoleptic Patients During Attacks of Sleep and Similar States.—In these experiments, as already stated, the patient sat in a quiet room, as free as possible from external stimuli. It was found that in this situation, most of the narcoleptic persons usually fell asleep within the first fifteen minutes. Since it was often difficult to tell when the patients were asleep it became a part of the routine of the experiment to observe their responsiveness to slight noises around the laboratory or to the irksomeness of their sitting posture. The relative depth of the sleep was judged according to the response elicited when their names were called softly.

The electrical records taken while the patients sat in the chair from thirty to ninety minutes or more showed the following features: 1. The short attacks of sleep which last just a few minutes and from which the patient can be readily awakened at any time are not accompanied by any changes in skin resistance. A similar result was obtained in experiments performed on a group of normal subjects who took

short naps during the afternoon. 2. In some cases both the palm-palm and the back-back resistance begin to increase immediately after the patient is placed in the chair and mount to a high level even before he begins to doze. The magnitude of the increase as well as the general consistency of the response seems to be proportional to the severity of both the cataplexy and the attacks of sleep. The narcoleptic child in whom both cataplexy and extreme somnolence were most frequent also showed the greatest increase in resistance. Two of her records are presented in figure 5. In the first, the back-back resistance increased steadily from 110,000 ohms at the beginning of the experiment at 9:45 a. m., to 590,000 ohms at the end. (A similar result was obtained on every other occasion, even when she sat for only a short time.)

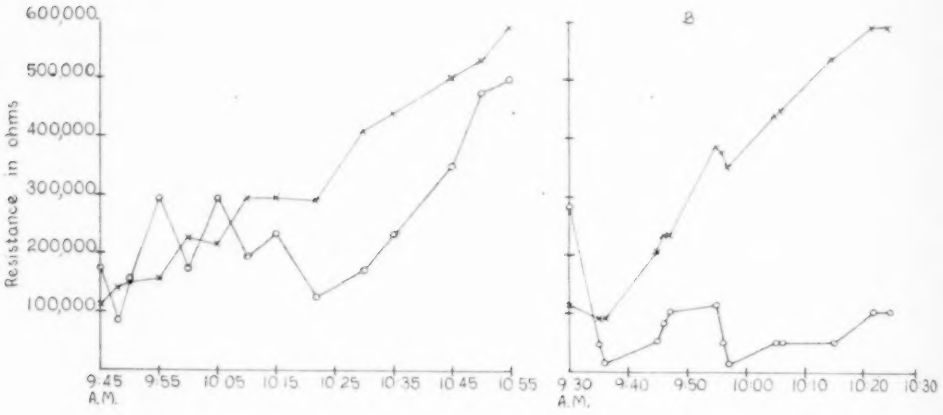

Fig. 5.—Two records of palmar and dorsal resistance showing changes that may occur on different days in the same narcoleptic patient within an interval of an hour. In *A*, a marked increase is shown in both the palmar and the dorsal curve. The patient was in a deep sleep at the end of this experiment. In *B*, the dorsal resistance increases while the palmar remains constant. The patient was awake throughout this experiment.

The palm-palm resistance also showed a marked increase, after a preliminary forty-minute period of marked fluctuation at a level considerably above the normal. At the end of the record, the patient was in a profound sleep. She did not fall asleep during the second experiment, but the record is characterized, nevertheless, by a striking increase in dorsal resistance and large fluctuations on the palmar curve. In all of the records of narcoleptic subjects, these peculiar fluctuations are more common in the palm-palm than in the back-back resistance.

These records contrast sharply with those obtained in the same situation on normal persons or on any other types of patients; in all of these subjects, the back-back resistance usually shows a sharp decrease

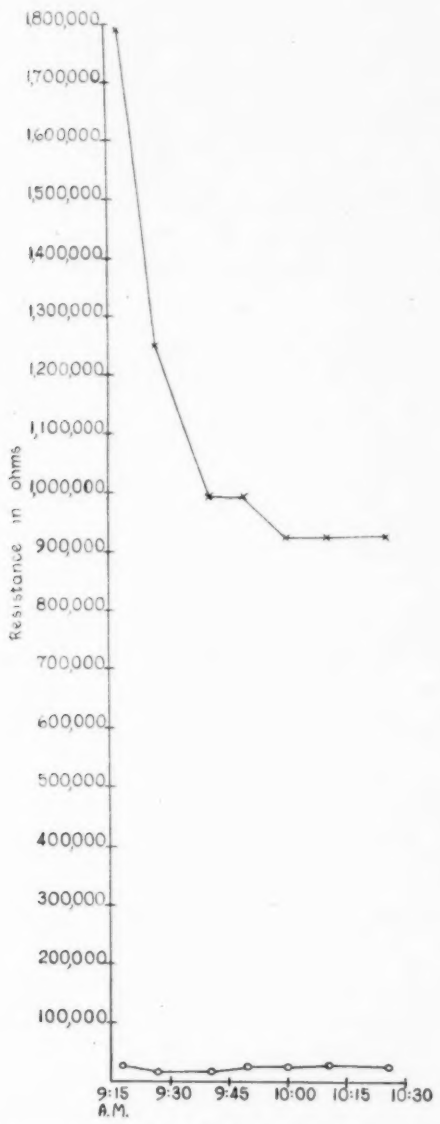

Fig. 6.—A typical record from a catatonic patient obtained under the same conditions as those prevailing when the records in figure 5 on a narcoleptic patient were taken. The palm-palm resistance remains on a flat level far below the normal.

rather than an increase, while the palm-palm remains fairly constant on its customary low level. The curves already shown can be contrasted with those in figure 6 obtained from a catatonic patient.

3. Records of Skin Resistance in Three Unusual Cases of Schizophrenic Stupor and Their Relation to the Records of Narcoleptic Patients.—It has already been stated that the large increase which occurs during the waking state in the palm-palm resistance of narcoleptic patients was not found in waking normal subjects and was found in only three of the many psychotic patients examined. These three patients were in a stuporous condition, apparently on a schizophrenic basis but with marked depressive features. A record from each of them is shown in figure 7.

CASE 4.—The first curve (fig. 7 *A*) was obtained from a woman, aged 28, whose illness began while she was teaching school. She became depressed, misinterpreted sounds and people and prayed a great deal. She twitched at night; she had right internal strabismus, the facial expression was masklike and the posture was rigid. Chiefly on the basis of the misinterpretations and because she thought she was hypnotized and pregnant, the patient was diagnosed as schizophrenic. The right knee jerk was considerably more active than the left, however, and she cried and moaned in an unusual rhythmic manner. Moreover, four years before admission to the hospital she had a high fever, was sleepy for several days and for some time afterward slept a great deal. Because the resistance records resembled those of narcoleptic patients and were in direct contrast to those obtained from other schizophrenic persons, one may conclude on the basis of what appears to be a history of encephalitis, that the organic facts played an important rôle in the condition. After several months the condition cleared up and she went home. She appeared then to be retarded rather than disturbed, and established fairly good contact with her surroundings.

CASE 5.—In this patient, a woman, aged 20, the condition was also diagnosed as schizophrenia with depressive features. On the anniversary of the death of her father, to whom she had been devoted, she fancied a change in the attitude of her friends and family toward her and talked of killing herself. She spent much time standing in one position staring straight ahead of her, had two stuporous episodes with ecstatic behavior and showed a prevalent depressive mood. There was no history of encephalitis in this case, but the patient showed a high daily average of palm-palm resistance with extraordinary fluctuations in the palm-palm curve when she sat in a quiet room for a few minutes (fig. 7 *B*). She went home after eleven months without any disturbed ideas though still slowed in her behavior and thought

CASE 6.—In a man, aged 26, the condition was diagnosed as a schizophrenic reaction with catatonic stupor complicated by syphilis. A year before he entered the clinic, he became frightened by a trifling incident which occurred one night as he was returning home. Subsequently he became depressed, prayed a great deal and repeated again and again, "There is no hope for the future." On admission he showed a retarded reaction to stimuli, spoke slowly in monosyllables, and sat listlessly, staring straight ahead with his head sunk on his breast and his arms hanging limply at his sides. After several months in a stuporous condition, he improved and went home. There was a vacant and somewhat painful expression on his face; the pupils were unequally dilated, and he had grandiose feelings and an idea that "the war had put a spell" over him.

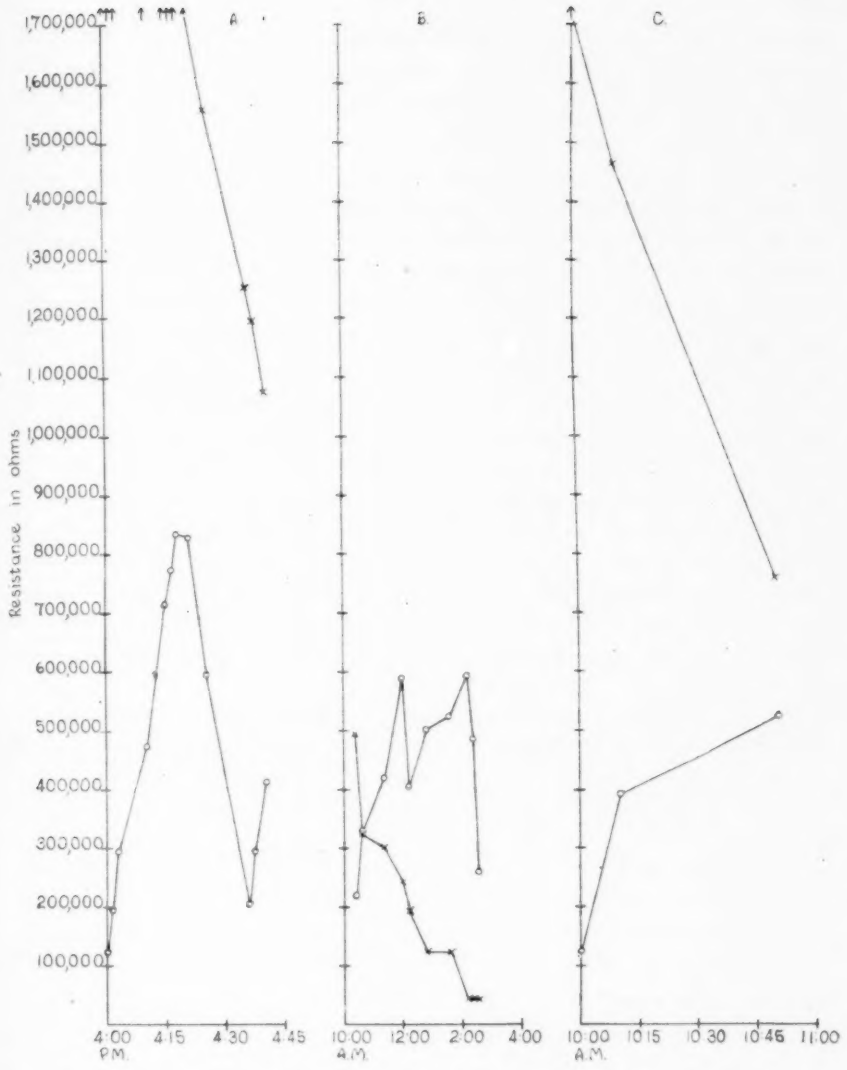

Fig. 7.—Skin resistance records obtained from three patients in whom the condition was diagnosed as schizophrenia with depressive features. These experiments were performed under conditions similar to those present during the records in figures 5 and 6. In *A*, the palmar resistance shows a great increase, far above the normal limits, with marked fluctuation as well. In *B*, the palmar level is high at the outset, and increases further, far above the normal limits. The palmar curve also shows unusual fluctuations. When it was highest, the patient seemed to be asleep. Unlike the narcolepsy records, the dorsal resistance was low at the outset and decreased as the experiment proceeded. The patient whose record is presented in *C* was in a deeper stupor than the other two. The palmar resistance rose rapidly from 120,000 to 530,000 ohms. As in the previous record, the dorsal resistance showed a precipitous drop. None of these patients showed any muscular disturbances like those present in the narcoleptic subjects.

This patient showed a high daily average of back-back resistance and a fairly high palm-palm average (fig. 7 *C*). His records are characterized moreover by a marked increase in palm-palm resistance during prolonged periods when he sat undisturbed, staring blankly ahead of him.

COMMENT

The records obtained in the present experiments on narcoleptic patients and other persons suffering from similar conditions show clearly that all of these patients are physiologically abnormal, even in the intervals between the somnolent and cataplectic attacks. All the narcoleptic subjects showed a high back-back and a relatively high palm-palm resistance with marked fluctuations in both, not only from day to day but even from moment to moment. The skin resistance records undoubtedly reflect a condition of great instability in the vegetative nervous system, which involves both the mechanisms that control sleep and those that control the tone of the skeletal muscles.

On the basis of the skin resistance records, one would say that the sleep during the short cataplectic attacks is not deep. This is consistent with the clinical observation that these patients can be quickly and easily aroused. Furthermore, on the basis of the records it can be said that a marked relaxation of the muscles often occurs during the attacks even when the subjects do not actually fall asleep.

It is particularly interesting to note that similar records were obtained from three patients with a condition that was diagnosed as schizophrenia. All these patients were semistuporous, and all showed marked depressive features in addition to the schizophrenic symptoms. The electrical resistance records during the stuporous state were in absolute contrast to those obtained from catatonic or other schizophrenic patients, in that the palm-palm resistance increased and remained high, whereas in catatonic patients it is consistently low. All three of these patients recovered enough to go home, but they were all somewhat dull and slowed. Two points may be significant for an understanding of these cases. There is the suggestion of Hoch[7] that some of the benign depressive stupors have much in common with normal sleep; there is also the possibility that these patients may actually have been suffering from some encephalitic process, and that the schizophrenic symptoms were only accessory or coincident factors.

It is obvious that a single record would be misleading in the foregoing experiments. In these examinations, as in so many others, it is necessary to obtain numerous readings at various times on each patient. The resistance method has a particular advantage in this connection over such clinical tests as the measurement of the basal metabolic rate in that readings of the electrical resistance can be repeated frequently without much effort or loss of time.

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7. Hoch, A.: Benign Stupors, New York, The Macmillan Company, 1921.

SUMMARY

1. The electrical skin resistance of five narcoleptic patients deviated from the normal in a number of ways:

(*a*) The average daily skin resistance was much higher in these patients than it is in normal persons, frequently being as high in the patients in a waking state as it is in normal subjects only during deep sleep.

(*b*) The resistance showed extraordinary fluctuations from one extreme to another from moment to moment.

(*c*) The resistance increased rapidly to a high level when the patient was left undisturbed in a quiet place for only a few minutes, whereas in normal subjects in a similar situation it tends to decrease.

2. Records from a patient with attacks of sleep, supposedly hysterical in origin, were similar to those obtained from narcoleptic patients. This fact, in addition to a previous history of high fever and diplopia, suggested that the attacks in this case were probably on a more definitely organic basis.

3. Records were presented also of three patients in a stuporous condition apparently of schizophrenic origin, but with marked depressive features. Because the records of these patients were so different from those usually obtained from schizophrenic patients, and because they resembled the narcoleptic records, it was suggested that the condition might be the manifestation of some disturbance of the sleep mechanism due to an encephalitic process. This theory would be consistent with the suggestion of Hoch that the depressive stuporous state may possibly be regarded as a pathologic disturbance of the normal sleep mechanism.

THE RELATION BETWEEN THE WASSERMANN REACTIONS IN THE BLOOD AND IN THE CEREBROSPINAL FLUID

A CONTRIBUTION TO THE QUESTION OF THE ORIGIN OF THE ANTIBODIES*

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The study of the question whether the production of antibodies is limited only to certain specific tissues (the hematopoietic organs) or whether it may take place in different tissues is important from both the biologic and the therapeutic point of view. If the ubiquitous origin were to be proved, it would be possible, as Ehrlich said several years ago,[1] to facilitate the process of immunity by inciting the formation of antibodies, not only in the important differentiated organs, but also in the nondifferentiated tissues, such as the subcutaneous tissue. As we shall show later, the assumption of the possible production of antibodies anywhere in the organism was admitted and proved experimentally, and it led to specific treatment in various diseases.

On the question of the origin of the antibodies that give the positive Wassermann reaction in the cerebrospinal fluid, two opinions have been advanced and will be discussed in this paper.

In view of the fact that in certain cases the Wassermann reaction is positive in the fluid and negative in the blood, the independent production of antibodies in the fluid is likely. It nevertheless appears doubtful when one considers the well known fact that the Wassermann reaction tends to be inhibited by proteins, and that therefore the cerebrospinal fluid is a rather more favorable medium for the Wassermann reaction than the blood with its great amount of proteins (70 per cent). This property of the serum was demonstrated many years ago by Friedmann,[2]

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* From the Clinic of Internal Medicine (Professor Roch) and the Psychiatric Clinic (Professor Ladame) in Geneva.

1. Quoted by Wassermann and Citron: Ueber die Bildungsstaetten der Typhusimmunikoerper. Ein Beitrag zur Frage der localen Immunität der Gewebe, Ztschr. f. Hyg. u. Infectionskrankh., 1905, no. 50.

2. Friedmann, N.: Experimentelle Untersuchungen zur Theorie der Wassermannschen Reaction, Ztschr. f. Hyg. u. Infectionskrankh., 1910, vol. 67.

and Zaloziecki,[3] among others; moreover, Friedmann noted that dilution of the serum eliminates the action of the proteins. On the ground of this fact, Dujardin [4] felt justified in asserting that the only seat of production of antibodies is in the blood; and that consequently the Wassermann reaction in the cerebrospinal fluid is due to the antibodies coming from the blood; finally, he stated that the passage of blood antibodies into the fluid is related to the inflammation of the meninges.

Before discussing this statement, we will submit our observations and the conclusions they warrant.

OBSERVATIONS

We have studied eighty cases, most of them bearing the diagnosis of general paralysis. There were included also cases of tabes, meningitis, hemiplegia and several other diseases of the nervous system. The syphilitic etiology was established in all.

As the accompanying table shows, we noted in each case the Wassermann reaction in the blood and in the cerebrospinal fluid, and the amount of albumin and the number of cells in the fluid, in order to be able to judge the degree of inflammation of the meninges. The intensity of the Wassermann reaction, when feeble, is noted by +; and when more pronounced, by + + and + + +.

COMMENT AND CONCLUSIONS

Study of the table shows that there are many cases, such as nos. 1 to 38, in which the Wassermann reaction is positive in the fluid and negative in the blood. We do not use this fact as an argument for the production of antibodies in the cerebrospinal canal, since we recognize that the statement quoted with regard to the inhibition of the Wassermann reaction by the blood proteins is well established. By dilution of the serum, it would perhaps have been possible in our cases to render the Wassermann reaction also positive in the blood. On the other hand, by comparing the Wassermann reaction in the cerebrospinal fluid with the degree of inflammation of the meninges, two facts are made clear: In cases 39, 40, 41, 42, 43, 44, 45 and 46, the Wassermann reaction is positive in the blood and negative in the fluid in spite of inflammatory reaction of the meninges as measured by the increase of albumin and by the presence of cells. Evidence is not found of a necessary relationship between the strength of the Wassermann reaction and

3. Zaloziecki, A.: Ueber den Antikoerpernachweis im Liquor cerebrospinalis, seine theoretische und praktische Bedeutung, Arch. f. Hyg. u. Infectionskrankh. **80**:196, 1913.

4. Dujardin, B.: L'index de perméabilité. Moyen d'établir le diagnostic et le pronostic des réactions méningées syphilitiques, Ann. d. mal. vén. **15**:129, 1920; Anticorps syphilitiques et perméabilité méningée, Bull. Soc. roy. d. sc. méd. et nat. de Bruxelles, July 7, 1914, vol. 72.

Comparison of the Wassermann Reaction in the Blood with That in the Cerebrospinal Fluid of Syphilitic Patients; Also Comparison of the Wassermann Reaction of the Cerebrospinal Fluid with the Inflammatory Reaction

No.	Diagnosis	Blood: Wassermann Reaction	Cerebrospinal Fluid: Wassermann Reaction	Cerebrospinal Fluid: Albumin per 1000 Cc.	Cerebrospinal Fluid: Leukocytes
1	General paralysis	0	+	0.56	3.5
2	General paralysis	0	+++	1.5	130
3	General paralysis	0	+++	0.50	51
4	General paralysis	0	++	0.48	30
5	General paralysis	0	+++	0.75	168
6	General paralysis	0	+++	0.70	17
7	General paralysis	0	++	0.50	27.8
8	General paralysis	0	++	0.15	2
9	General paralysis	0	+++	0.50	48
10	General paralysis	0	+	0.56	2
11	General paralysis	0	+++	0.65	10
12	General paralysis	0	++	0.60	46
13	General paralysis	0	++	0.25	....
14	General paralysis	0	+++	0.40	130
15	General paralysis	0	+++	0.50	50
16	General paralysis	0	+++	0.55	36
17	General paralysis	0	+++	0.35	4
18	General paralysis	0	+++	0.90	74
19	General paralysis	0	+++	0.45	660
20	General paralysis	0	+++	0.56	30
21	General paralysis	0	+++	0.50	42
22	General paralysis	0	+	....	57.2
23	General paralysis	0	+++	1	200
24	General paralysis	0	+	0.50	1
25	Tabes	0	+	1.0	36
26	Tabes	0	+	0.25	33
27	Syphilis	0	+	0.50	88
28	Syphilitic meningitis	0	+	0.15	20
29	General paralysis	0	+++	0.50	5
30	Tabes	0	+	0.10	1.6
31	Tabes	0	++	0.25	320
32	Tabes	0	+	0.34	21
33	Tabes	0	+++	0.63	10
34	General paralysis	0	+++	0.71	206
35	General paralysis	0	+	0.40	9.6
36	General paralysis	0	+++	0.40	8
37	General paralysis	0	+++	0.71	44
38	General paralysis	0	++	0.20	123
39	Syphilis; paranoid ideas	++	0	0.56	12
40	General paralysis	+	0	0.75	122
41	Syphilitic meningitis	+	0	1.30	290
42	Thalamic syndrome syphilis	+	0	0.25	15
43	Cerebral syphilis	+++	0	0.15	15
44	Hemiplegia	+	0	0.75	122
45	Tabes	+++	0	0.25	15
46	Syphilitic meningitis	+++	0	0.25	64
47	General paralysis	+	+++	0.50	55
48	General paralysis	+	+++	0.65	26
49	General paralysis	0	+	0.65	2.3
50	General paralysis	+	++	0.45	30
51	General paralysis	+++	+++	0.50	2.80
52	General paralysis	+++	+++	1.0	171
53	General paralysis	+++	+++	....	72
54	General paralysis	+++	+++	0.90	54
55	General paralysis	+	+	1.5	103
56	General paralysis	+++	+++	0.40	4
57	General paralysis	+++	+++	0.45	26
58	Syphilitic hemiplegia	0	0	0.61	....
59	Tabes	+++	+++	1.0	14
60	Syphilitic meningo-encephalitis	0	+++	0.15	0.4
61	Cerebral syphilis	0	+	0.15	2
62	Tabes	0	0	0.60	18
63	Tabetic stomach pains	0	0	0.40	9
64	Tabes	+	++	0.50	17
65	Tabes	++	++	0.20	13
66	Syphilitic neuralgia	+	+	0.2	101
67	Syphilitic meningo-encephalitis	+	+++	0.20	24
68	Cerebral syphilis	+	+	1.5	35
69	Syphilitic meningitis	+	+	0.25	10
70	Syphilitic meningitis	+++	+++	....	575
71	Syphilitic radiculitis	+	+	0.25	4.8
72	Syphilitic neuritis of the trigeminal nerve	+	+	1	78
73	Syphilitic meningitis	+++	+++	1.2	246
74	Tumor of brain	+++	0	0.10	0.5
75	Syphilitic encephalomyelitis	+++	+++	0.78	19
76	Tabes	+++	+++	0.75	33
77	Tabes	+++	+++	0.60	44
78	Tabes	+	+	0.50	16
79	Hemiplegia; syphilis	+	+	2	193
80	Syndrome of the globus pallidus	+++	+++	0.25	67

that of the inflammatory reaction in the fluid. There are cases in which a +++ Wassermann reaction in the fluid is accompanied by a small amount of albumin and a small number of cells. On the other hand, in many cases, much albumin and a great number of cells appear together with a feeble Wassermann reaction.

Thus, even if we admit for a moment that the antibodies of the fluid come from the blood, we do not agree with Dujardin that the quantity of antibodies in the fluid could give information as to the severity of the inflammation and consequently the degree of the permeability of the meninges. The so-called index [5] of permeability established by Dujardin may not have the significance that he attributes to it.

As we had occasion to show in a study of the influence of aseptic meningitis on the meningeal permeability,[6] the latter is capricious in regard to sodium nitrate; it is not less capricious in connection with the antibodies. But it would be a mistake to assume that the blood is the only source of the antibodies. At any rate, neither the material on which Dujardin and other writers on the subject founded their statements nor our own observations authorize such a conclusion. Why could one not admit, instead of the passage of antibodies from the blood into the fluid, a current in the contrary direction, or currents from both directions? The antibodies produced in inflammatory tissues in the cerebrospinal canal may pass into the blood. There seems to be more reason for admitting such a phenomenon because the following fact is well established: whereas most substances introduced into the blood do not pass, under physiologic conditions, into the cerebrospinal fluid, the passage in the opposite direction is easy.

If one were allowed to reason by analogy, one could admit the local production of antibodies in the cerebrospinal canal as the formation of specific antibodies in the skin was demonstrated by Bloch and Massini, Wolff-Eisner, Dubi and Sahli,[7] and in the pleura, the peritoneum and the subcutaneous tissue by Wassermann and Citron.[1] This phenomenon was proved also by the interesting experiments of Bruno Fellner,[8] who was able to demonstrate the presence of the specific antibodies against tuberculin in papules produced by Pirquet's reaction.

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5. When we designate by n the highest dilution of the cerebrospinal fluid, and by N the highest dilution of the blood that will give a positive Wassermann reaction, n/N would be the index of permeability.

6. Katzenelbogen, S.: De l'augmentation de la perméabilité méningée aux nitrates dans la méningite, aseptique provoquée, Schweiz. med. Wchnschr. **54**:833, 1924.

7. Sahli, H.: La tuberculinothérapie et le traitement intradermique, Paris, A. Maloine, 1922; Ueber Tuberkulinbehandlung mit besonderer Berücksichtigung der Intrakutanbehandlung, Schweiz. med. Wchnschr. **50**:557, 1920.

8. Fellner, B.: Wien. klin. Wchnschr. 1919, no. 38, p. 936.

By inoculating persons who did not originally react to tuberculin with the serum of these papules, he rendered these persons sensitive to tuberculin. We may mention, by the way, that on account of this property the skin has been used by Sahli and others in the treatment with tuberculin.

It is obvious that we are not justified in drawing conclusions from what happens in the skin as to what would take place in another part of the organism, such as the cerebrospinal space. The only right way is to prove the formation of antibodies in the cerebrospinal space itself. This was recently done by Muttermilch [9] in Pasteur's Institute in Paris. He found that the injection of the red cells of sheep into rabbits intravenously, subcutaneously and into the peritoneum produced hemolysins against sheep cells in the blood but not in the cerebrospinal fluid; and that the introduction of sheep cells into the cerebrospinal canal, on the other hand, promoted the formation of hemolysins in the fluid and also in the general circulation. In order to show that the antibodies in the fluid were produced in the canal and did not come from the blood through the meninges, which might be damaged by a puncture, Muttermilch made several punctures and injections of blood of guinea-pigs into the spinal canal of rabbits which were immunized against sheep red cells. In these experiments, he did not find hemolysins against sheep cells in the fluid.

In many other experiments, by inoculating rabbits with cholera and typhoid bacilli by way of the cerebrospinal canal and the peritoneum, Muttermilch showed in the fluid the specific antibodies only in cases in which the microbes were introduced into the cerebrospinal canal.

These experiments are encouraging and justify the attempts at active immunization of the cerebrospinal fluid which Gilbert and Tzanck [10] made previous to these experiments, using the vaccine of Levaditi and Poincloux in epidemic encephalitis.

On the other hand, when we admit with Sahli that every albuminoid substance is, because of its colloid constitution, able to call forth the production of antibodies, we find in this a partial explanation of the beneficial results which we obtained in epidemic encephalitis by injecting casein into the cerebrospinal canal.[11]

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9. Muttermilch, S.: L'immunisation active de la cavité méningée, Compt. rend. Soc. de biol. **95**:945, 1926; Immunité antimicrobienne de la cavité méningée, ibid. **96**:397, 1927.

10. Gilbert, A., and Tzanck: Encéphalité léthargique; traitement par le virus vaccin encéphalitique par voie intra-rachidienne (Méthode de Levaditti-Poincloux), Soc. méd. d. hôp. de Par. **48**:541 (April 11) 1924.

11. Roch, M., and Katzenelbogen, S.: Traitement des formes évolutives chronique de l'encéphalite épidemique par les injections intrarachidiennes de caséine, Schweiz. med. Wchnschr. **54**:834, 1924.

CHONDROMYXOSARCOMA OF THE SIXTH CERVICAL VERTEBRA*

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Chondromyxosarcoma is a rare form of vertebral tumor, judging from the lack of any reference in the recent literature to this type of lesion. The statistics of Schlesinger show 107 vertebral tumors in 35,000 autopsies (0.32 per cent), while the records from the Heidelberg Clinic, reported by Holm,[1] show 14 vertebral tumors in 4,700 autopsies from 1921 to 1926, or 0.29 per cent. Of these, only 2 were chondroma. Chondroma of the vertebra is rare, but chondroma of other bones appears to be not unusual. In 18 cases of chondroma observed during a period of seven years at the Mayo Clinic, none was vertebral, while in the 237 cases of chondromas reported by Weber only 1 was located in the vertebral column. None of the investigators report any cases of primary chondromyxosarcoma of the vertebra.

In the case which is the subject of the present discussion, the tumor had its origin in the body and intervertebral disk of the sixth cervical vertebra.

An unusual clinical feature was the long duration of the vertebral disease without producing the symptoms commonly associated with such lesions. There was never any local tenderness or rigidity of the cervical spine, and only after several months were symptoms of the sensory root observed. The atrophy of the small muscles of the hand, the fibrillary tremors in the atrophied muscles and the spasticity of the lower extremities led to the diagnosis of amyotrophic lateral sclerosis until the sensory changes and symptoms referable to the bladder had developed to a degree which indicated that this diagnosis was in error.

REPORT OF CASE

History.—T. L., aged 33, single, a farm laborer, was admitted to the Buffalo City Hospital on Feb. 19, 1926, the chief complaints being: (1) extreme weakness and loss of power in the legs, (2) weakness and loss of power of the left arm with atrophy of the muscles, (3) beginning weakness of the right arm, (4) some difficulty in emptying the bladder and (5) cough of three months' duration.

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* Submitted for publication, May 25, 1928.

* Read at the Fifty-Fourth Annual Meeting of the American Neurological Association, Washington, D. C., May 1, 2 and 3, 1928.

1. Holm, H.: Deutsche Ztschr. f. Chir. **208**:46 (Jan.) 1928.

The onset of weakness in the left hand gradually progressed to the forearm and for a while was accompanied by pain and paresthesias along the ulnar side of the extremity. This was relieved by hot poultices, but the pain then appeared temporarily in the right shoulder. About two weeks before the patient was admitted to the hospital, the legs became weak and later he lost the ability to stand. He had been up and about until a few days previous to admission. Symptoms of the bladder were beginning to develop, and the hesitancy in urination required relief by hot applications over the abdomen. Some cramps were observed in the muscles of the legs for several days, but the twitching and fibrillary tremors had been present for a number of months. The family and personal history was without significance, except that the mother had died of a tumor of the uterus.

Examination.—The pupils were unequal, the right larger than the left; they reacted well to light and in accommodation. Some nystagmoid jerkings of the eyes were noted when the patient looked toward either side. The disks and blood vessels of the fundi were normal. The other cranial nerves were normal.

Atrophy was present in the muscles of the shoulder girdles and was more marked on the left. Atrophy was also present in the small muscles of the left hand. The thenar muscles and the first dorsal interossei were markedly wasted and showed fine fibrillary tremors. There was a loss of all movements supplied by the ulnar nerve, with a claw hand on the left. There was fairly good power in the biceps and triceps groups, and the musculospiral nerve function was good. Some weakness was developing in corresponding muscles on the right. There was spasticity of the lower extremities. The knee reflexes and ankle reflexes were exaggerated, and ankle clonus was present. A Babinski toe sign was present on both sides.

There was no rigidity of the spine in any segment. The abdomen was held rigid, and the abdominal reflexes were not obtained. The intercostal muscles were weak, and coughing was difficult.

The spinal fluid did not show an increase in pressure; it was clear and did not show a yellowish tinge; there were *2* cells per cubic millimeter, a slight increase in globulin as shown by the Ross-Jones and the Pandy tests, a negative Wassermann reaction and a colloidal gold curve of 0001221000.

The examination of the blood showed: red cells, 4,800,000; hemoglobin 85 per cent; white cells 5,200; polymorphonuclears 75 per cent; small lymphocytes 14; large lymphocytes and large mononuclears 10, and eosinophils 1 per cent.

The heart did not show any abnormalities at the time of admission. Râles were found scattered throughout the chest, especially in the upper lobes.

A report of the x-ray examination of the chest stated that: The pulmonary fields on both sides showed considerable infiltration with fibrosis. The right side, under the fifth and sixth ribs posteriorly, in the outer zone of the lungs, showed an area of increased density, having diameters of *2* by 3 cm. The diagnosis of this area should be made only in consideration of the clinical observations, with the possibility of metastases in mind.

Course.—After a few days in the hospital, the symptoms referable to the bladder became troublesome, and catheterization was necessary. The lungs developed diffuse bronchopneumonia and cardiac failure became progressive. The general symptoms became so severe that further neurologic studies were interrupted, although evidences of disturbed objective sensibility were found in the lower extremities. Loss of temperature sensibility and delayed pressure sensibility, with absence of muscle and joint sense, were demonstrated in the lower extremities. Tactile discrimination was well retained in the feet.

On March 27, there was a rapid increase in the pulmonary symptoms with acute cardiac failure resulting in death.

Autopsy Report.—The body was 5 feet 5 inches (165 cm.) in height; the weight was estimated at about 120 pounds (54.4 Kg.). Atrophy of the muscles of the extremities, especially of the muscles about the thumbs and the interossei was present. A large decubitus ulcer was present over the sacrum.

On removal of the calvarium, the cerebrospinal fluid was found increased in amount. The cut surfaces of the brain appeared wet, but on careful dissection neither areas of softening nor of induration were found. The pineal and pituitary bodies were normal. The pons, cerebellum and the cerebral hemispheres were normal.

When an opening was made into the spinal canal from the occiput downward to the level of the iliac crest, a distinct tumorous encroachment was found, in the lower cervical region, on the spinal canal extending more from the right lateral side but also posterior and from the left lateral side. Removal of the spinal cord showed it to be distinctly compressed, and some of the material from the tumor was adherent to the dura but did not penetrate it. The extent of this tumorous invasion of the spinal canal was from the sixth cervical to the second dorsal vertebra. On removal of this segment of the cervical and dorsal vertebrae, including the lower four cervical and the upper four dorsal, and bisecting it, the entire vertebral body of the sixth cervical was found involved by the tumor mass. Apparently it had radiated out from this point up and down the spinal canal.

The tumor, on section, had a peculiar boiled-rice appearance and was extremely friable. It had a somewhat translucent appearance and broke down readily under the palpating finger. On the anterior portion of the bodies of the vertebrae, at the upper dorsal and lower cervical level, there were several confluent nodules about the size of small cherries which projected forward.

The larynx, trachea, tongue, tonsils, thyroid and the entire course of the esophagus appeared normal.

The heart was of average normal size and shape; the musculature was pale and slightly flaccid. There were some areas of thickening and induration of the mitral leaflets without encroachment on the orifice. The foramen ovale was fenestrated, with multiple openings varying in size from that of a pinhead to that of the tip of the little finger.

The lungs were both voluminous and did not collapse on removal of the sternal breast-plate; on exploration of the pleural space on the left side a considerable quantity of dirty, greenish, foul-smelling pus was set free, apparently from the lungs. Palpation of the lungs revealed numerous nodular areas, varying in size, and one nodule in the upper left lobe the size of a small apple. These nodules, on section, showed the same characteristics as the tumor masses in the spinal canal. Section through the lungs showed these metastatic tumor nodules to vary in size from that of a small pea to that of a large horse-chestnut. The lymph nodes in the hilum and the peribronchial lymph nodes were free from tumor metastases.

Metastases were not found in any of the abdominal viscera and except for slight incidental changes in some of the viscera they were practically normal.

Histologic Report.—A section of the decalcified cervical vertebra, including the intervertebral disk and almost half of the body of the vertebra, showed a large nodule, rather elliptic in shape, in the central portion of the intervertebral disk, and from this nodule the tumor cell elements could be traced directly out to the spinal canal. The spaces in the cancellous bone were all filled with necrotic tumor

masses, the bone lamellae appeared in part to be undergoing absorption, and some of the spaces showed friable tumor cells. The necrotic tumor masses filling these spaces were in the form of a fine reticulum that stained rather diffusely with eosin and was without nuclear elements. Other circumscribed areas were also seen along the edges and in the periosteum that did not show tumor cell elements but did show an extremely fine reticulum that gave a multiloculated appearance, which took a pale blue stain rather than the eosin. There were also areas in which the tumor cells were more clearly defined, showing both protoplasm and nucleus and the irregular squamous cells showed a delicate protoplasmic process giving rise to this fine reticulum. These often had a stellate appearance. The tumor cell masses seemed to be devoid of any particular stroma, except such as was created by the tumor cell masses themselves. Vascular structures did not appear to be a part of the tumorous proliferation. There were not any mitotic figures, but many cells appeared to be distinctly paired, suggestive of an amitotic form of division.

The tumor nodule that was found at the outer side of the dura, and the nodules found in the lungs also showed this fine reticulated appearance. They stained deeply with hematoxylin, taking a peculiar vacuolated appearance; in many of these situations the protoplasm appeared to be breaking down and giving rise to vacuolation.

In the lung the tumor nodules appeared to be regularly and consistently inside the blood vessels, especially the smaller nodules, but there were also some inside the bronchi. In the latter situation it appeared that by pressure erosion, as the tumor nodules grew, it broke down the walls and thus invaded the bronchi. In none of the numerous situations in the lungs did it appear to infiltrate the surrounding tissue directly, but appeared to spread by pressure erosion and breaking down of the barriers. This was also clearly shown in the spinal canal in which the tumor cell masses were definitely outside the dura and did not show an invasion of the dura.

COMMENT

In the attempt to classify the unusual histologic character of the tumor, some of the slides were sent to Dr. F. V. Mallory, of the Boston City Hospital, who looked over the specimens and made the diagnosis of chondromyxosarcoma. He said that Prof. J. M. Stewart, of Leeds, England, also agreed with this diagnosis. A number of the tumor slides were also submitted to the inspection of Professor Ghon, at Prague, who agreed that the tumor could be classified as a chondromyxosarcoma.

As shown by the observations made at autopsy, the possibility of surgical removal of the tumor in the spinal canal presented many difficulties, although decompression and removal of portions of the mass might have been accomplished. The absence of secondary degenerative changes in the spinal cord indicated that considerable restoration of function might have resulted if the metastases in the lung had not been present. Holm [1] recently reported a case of simple lobulated chondroma in which numerous round tumor masses of bony consistency, the size of a hazelnut, were successfully removed from the region of the third and

fourth cervical vertebra. The tumor masses had compressed the cord flat but had not broken through the dura. At the end of one year after the operation, complete recovery of function had occurred.

SUMMARY

A vertebral tumor of the type of a chondromyxosarcoma of the sixth cervical vertebra and intervertebral disk, which produced compression paraplegia with the clinical symptoms, at the onset, of amyotrophic lateral sclerosis was presented. The spinal cord showed marked flattening from pressure outside the dura but not any degeneration of any portions of the structure of the cord. Multiple metastases were present in the lungs which showed tumor masses of the same character as that found in the vertebra and spinal canal.

RECURRENCE OF STUTTERING FOLLOWING SHIFT FROM NORMAL TO MIRROR WRITING*

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A number of previous writers have noted that stuttering has followed enforced training of a naturally left handed child to write with the right hand, but I do not know that any one has reported cases of stuttering following a change from writing in the ordinary form to the mirrored form. The following case report concerns an adult with a severe grade of writing disability who began to stutter shortly after he undertook to substitute the mirrored form for the ordinary form of writing.[1]

REPORT OF CASE

History.—The father had a writing disability; if he wrote very slowly, the writing was legible; as a rule, he held a pencil in either the right or the left hand, although lately he had been holding it between the two thumbs and two forefingers, but not in either hand. The patient's maternal uncle, notwithstanding that he had an excellent mind and was considered an able criminal lawyer, had never learned to write; he was right-handed and did not present any speech abnormalities. The patient's older brother also had difficulty in learning to write; although he had spent hours diligently practicing, he was still a poor writer. He was right-handed, and had always been skilful with his fingers. No one in the family was known to have had any mental defect, disease or noticeable left-handedness.

W. D. seemed to have been a normal, typical middle western boy with the usual interests in studies and sports. He walked at the age of 1 year and talked at 18 months. During infancy he showed a preference for the right hand in reaching, holding and throwing. When he began to feed himself and to write, he used the right hand. Infantalalia, coupled with rapid and indistinct speech, persisted unduly. He stuttered "badly" when about 12 years of age. He had made good grades throughout his school career. Since entering the university he had become slightly introvertive and had developed irregular habits. Although never a fluent talker, none of his university teachers or acquaintances had ever noticed him stuttering. He had had enormous difficulty in learning to write. Although concentrating on penmanship even to the point of including it in his college curriculum, he had not made any improvement.

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* The work here recorded was carried out in the laboratories of the Iowa State Psychopathic Hospital as part of a program of research in physiology of the brain which was supported by a grant from the Rockefeller Foundation. Additional funds have also been supplied by the Graduate College of the State University of Iowa.

* This study was made when the writer was a Fellow of the National Research Council.

1. Brief mention of this case has been made by Orton, S. T.: Hygeia **5**:451 (Sept.) 1927.

When this study was made, the patient was a junior medical student, 25 years of age. It was impossible for his teachers to read his examination papers, and he was therefore required to read them to his instructors. However, he admitted that he could not read his own writing, and he depended on his memory to relate what he had intended to write.

As a rule, he formed the first letter of a word correctly and began each sentence more legibly, but as he proceeded the writing became progressively worse. Capital *I*, small *r* and *s* caused him especial trouble. He left out many letters, interpolated extra ones and reversed the order of others. He possessed average ability to spell orally. He detected misspelled words in proof reading, but did not notice them in his own productions.

In spite of this writing disability, which made it necessary for him to rely on other students' lecture notes, and many oral examinations he ranked tenth in a class of seventy-five.

Examination.—Figure 1 presents a sample of the writing at the time this study was begun.

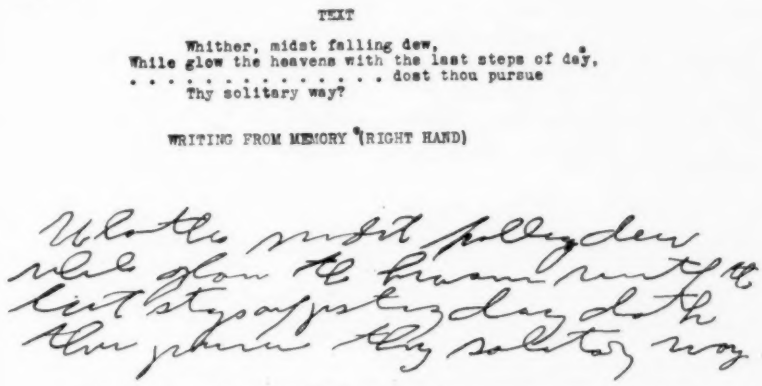

TEXT
Whither, midst falling dew,
While glow the heavens with the last steps of day,
. . . . . dost thou pursue
Thy solitary way?
WRITING FROM MEMORY (RIGHT HAND)

Fig. 1.—Sample of writing at the time the study was begun.

It was discovered that the patient was essentially ambidextrous. He threw, shaved and combed his hair with either hand; ate with the left, and wrote with the right. He used the left eye in unilateral sighting of binocular vision. Action current studies[2] revealed that of nine simultaneous voluntary contractions of both forearms the action currents appeared first only once in the right arm, first four times in the left, and simultaneously in the two arms three times. These observations corroborated the observation based on the ordinary criteria for handedness that this man lacked a preferential unilateral manual lead. Figures 2 and 3, respectively, show a left lead and a simultaneous lead.

With eyes closed, writing simultaneously with both hands, he furnished some interesting productions. He paused from five to thirty seconds before he began to form the letters. When he was permitted to look at the finished products, he appeared puzzled and traced imaginary lines in an effort to determine how he should have made them. With both pencils in position to write, he swayed from

2. A more complete description of the method used for this phase of the analysis is given in an article by Orton, S. T., and Travis, L. E.: Studies in Stuttering: IV. Studies of Action Current in Stutterers, Arch. Neurol. & Psychiat. **21:** 616 (Jan.) 1929.

side to side, backward and forward, giving the impression that he was making a great effort to begin.

The four possible combinations resulting from writing simultaneously with both hands are: (1) both hands may make the letter in the usual way; (2) both may produce the mirrored form; (3) the right hand may make the mirrored form and the left the usual, or (4) the right hand may produce the usual form and the left the mirrored. These four possibilities are shown in figure 4, with arrows to indicate the direction of progress. The patient, besides furnishing all four combinations, formed some letters upside down.

Figure 5 gives tracings of two productions when he wrote with both hands simultaneously.

Early in the study, he produced spontaneously with the right hand the mirror writing shown in figure 6. I was so surprised at the facility he displayed and the legibility of the product that I questioned him closely in regard to previous attempts or practice along this line. He emphatically denied that he had ever tried to produce mirror script before. Since further trials clearly demonstrated that he wrote in the mirrored form with greater speed and ease than in any other, I

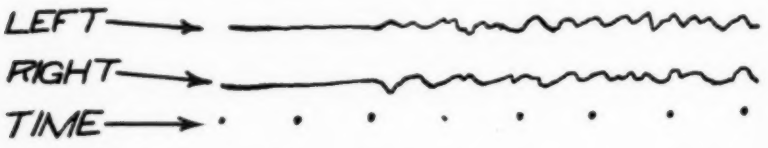


Fig. 2.—Tracings of a photograph of action currents from the forearms showing a left lead. Time is indicated in sixtieths of a second.

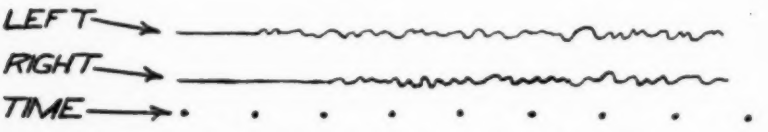
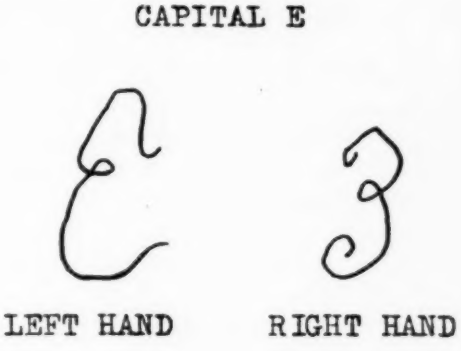


Fig. 3.—Same as figure 2 except that this shows a simultaneous lead.

advised him to adopt this method of writing exclusively. I suggested that he make his productions legible to others by placing a piece of carbon paper upside down beneath the sheet on which he was writing. His mirrored writing was thus copied in reversed form (the usual form) on the back of the sheet on which he was writing, and on turning over the sheet it could be read as ordinary writing.

For three days he wrote a great deal in the mirrored script, in taking notes, copying from others' notebooks, and practicing writing the alphabet. When he came to the laboratory on the fourth day, he presented such marked stuttering that he was scarcely able to talk. He displayed both blockings and repetitions. A study of his feelings, emotions and behavior for the immediately preceding period did not reveal anything of importance. He had been carrying on his regular routine of study in his customary way. However, on the fifth day after he had begun to write in mirrored form, he reported that he was becoming markedly confused in regard to the orientation of certain letters. He proceeded to write capital *B* in both the ordinary and in the mirrored form, saying that he did not know which was which. This confusion and stuttering persisted for approximately a month, during which he found it difficult to copy from a book but easy to write original productions. As he put it: "Anything in my head I can write easily, but

Fig. 4.—The four possible combinations resulting from writing simultaneously with both hands.



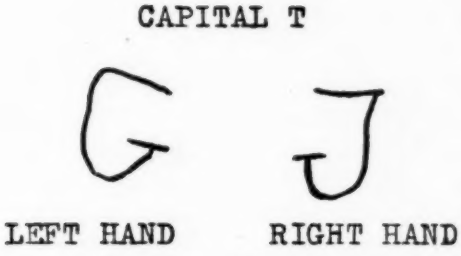


Fig. 5.—Samples of productions in writing simultaneously with both hands.

when I see it on the page it's harder. The stuff on the page has to go through my mind first." Early in the second month of mirror writing, the stuttering disappeared without returning.

COMMENT

The production of mirrored script for three days followed by a recurrence of stuttering presents an apparent causal-sequential relationship. In such a relationship, it is rarely possible to rule out absolutely the element of chance occurrence, but as the patient had not been stuttering before he wrote in the mirrored form and ceased to stutter after he had the new writing habits firmly established, it is probably safe to assume a real connection between the mirrored writing and stuttering. In attempting then to explain how the mirrored writing might have produced the stuttering, the emotional factor should be taken into consideration. For the average person, the affective reactions which might be expected to accompany such reorganization of writing habits as writing in mirrored form necessitates would possibly have some influence on behavior. Whether or not the effect would be great enough to interfere with proper functioning of the speech apparatus is a question. With

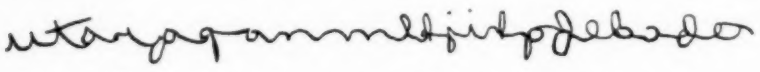


Fig. 6.—The first attempt to produce mirror writing.

this man, who found mirror writing so natural and easy, I believe that it is possible practically to rule out the emotional element.

Another explanation of the apparent relationship between stuttering and writing in mirrored form occurs to me. Previously recorded cases of stuttering indicate that speech is closely associated with the use of the hand, especially in manual signs and writing. In most persons, articulate speech is related to right-sided manual speech (writing). The associative patterns that serve these two functions are built up in the dominant hemisphere to produce in the peripheral expressive mechanisms a certain orientation and configuration. However, the two cerebral hemispheres have equal anatomic access to the midline structures subserving articulate speech, and either may control it. As the motor expression of one side of the brain is antitropic to that of the other side, it is seen that if the control alternates between the two hemispheres or comes from both at the same time, a distortion in the response of the midline structure of articulate speech might result.

In my case articulate speech had been associated with writing of the usual orientation, that is, to the right, although it is obvious that a close bond had not been established between them. When the man began to write in mirrored form, a new pattern was probably brought into action,

and it seems logical to assume that since this pattern was the mirrored reversal of its predecessor, it was resident in the other cerebral hemisphere. Thus one may envisage the occurrence of the speech disturbance as due to a conflict between the two hemispheres, comparable to that which frequently occurs when right-handed writing is forced on a left-handed child. Once the new form of writing was mastered and definitely established in the new direction, this conflict disappeared, and the stuttering also stopped.

MOTOR PHENOMENA IN SCIATICA*

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To the present day, the motor phenomena in sciatica have been insufficiently investigated. In studying and writing about sciatica, attention has been concentrated exclusively on the symptoms of pain and on the sensory phenomena, and it is commonly considered that neuralgia of the sciatic nerve leaves the motor functions entirely or almost entirely undisturbed. Yet, in reality, this is not true; there is a whole series of motor phenomena in sciatica which deserve to be looked into as being of great diagnostic importance.

SIGNS AND SYMPTOMS

The only motor symptom mentioned by some authors in describing sciatica is the Kernig sign. This sign is not infrequently mistaken for the Lasègue sign; some authors (Levandovsky, Oppenheim, Klieneberger, Alexander [1] and others) have regarded these symptoms as identical. Apparently this is due to the fact that in sciatica, Kernig's sign manifests itself mostly in the affected extremity, in which one also finds the Lasègue sign; the degree of the former always corresponds to the degree of the latter, and with decrease and disappearance of the Lasègue sign, the Kernig sign disappears also. On the other hand, the Lasègue sign may nearly always be seen in persons with cerebrospinal meningitis (epidemic, tuberculous and other kinds). The simultaneous presence of both signs points to a genetic connection; they should not, however, be considered as identical. The Lasègue sign is a symptom of pain connected with the sensory neuron, whereas the Kernig sign is a motor phenomenon connected with irritation or reflex heightening of excitation in the motor neuron.

In 1907, Bechterew [2] described the following phenomena in sciatica: The patient, when sitting up in bed, flexes the affected leg at the knee (Kernig sign); if he is made to stretch out the affected leg, he flexes the unaffected one. He is unable to stretch out both legs at once, but he is able to stretch each leg in turn. This phenomenon can be observed in cases of acute sciatica and disappears gradually with the lessening of the pains. In its essence, this phenomenon is that of the Kernig sign, which increases or decreases under the influence of the stretching or of the flexing of the unaffected leg.

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* From the Babuchin Hospital, formerly the Old Catherine Hospital.

1. Alexander: Ztschr. f. d. ges. Neurol. u. Psychiat., vol. 79.
2. Bechterew: Neurol. Centralbl. **26**:1107 (Dec.) 1907.

The symptom described by Bechterew is of great diagnostic significance; yet until now it has never been mentioned anywhere in the descriptions of sciatica, and clinical practice does not take it into consideration.

There are other motor phenomena that I have had occasion to observe in certain cases of sciatica [3] which have not yet been described, so far as I know. These symptoms, as well as the Kernig and Bechterew signs already mentioned, are connected with symptoms of pain, or rather they appear simultaneously with sensations of pain.

The first of these symptoms was observed when the Lasègue contralateral sign was provoked; the second occurred together with the Lindner [4] sign, which I have named the symptom of "the flexing of the head."

To render the description of these phenomena easier to understand, I shall briefly point out the sensations of pain with which they manifest themselves. The Lasègue contralateral sign (Montaud-Martin) consists of the following: the raising of the nonaffected stretched leg brings on pain on the affected side, mainly in the ischiatic area—tuber ischiaticus—sometimes in the lumbar region, and sometimes down the entire leg.

Flexing the head (the Lindner sign) occurs as follows: If enforced passive flexion of the head to the chest is effected in a recumbent or sitting posture with outstretched legs, pain arises in the lumbar region, in the ischiatic area, and sometimes down the entire leg on the affected side. In acute cases this symptom is clearly manifested in a recumbent posture; in subacute cases it may fail to appear, but it will do so if the patient is made to sit up in bed with the legs outstretched.

The Lasègue contralateral sign and the flexed head sign are tokens of root sciatica.

In regard to motor phenomena, if the nonaffected extended leg is raised, as is done when the Lasègue contralateral sign is provoked, pain will arise in the affected leg simultaneously with the flexing of the knee joint and of the hip joint. The more pronounced the contralateral Lasègue sign, i. e., the greater the pain elicited, the larger will be the angle of flexion of the knee. In subacute cases one may sometimes observe a slight flexing of the leg, or, at the least, even in the absence of sensations of pain, a marked tension of the musculature. With diminution and disappearance of pain, the symptom vanishes. This symptom is evidenced exclusively in cases of root sciatica of diverse origin.

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3. Schambouroff: Primary and Secondary Sciatica, Moscow, 1928 (Russian).
4. Lindner: Neurol. Centralbl. **36:** 534 (July) 1917.

The second symptom is connected with that of bending the head. If a forced, passive flexion of the head to the chest is effected while the patient is lying in bed with outstretched legs, the leg will flex, in the manner recounted, simultaneously with the arising of pains in the lumbar region and leg. In acute cases, this phenomenon is well manifested in a recumbent posture; in subacute ones it is absent, but in the recumbent posture the flexion of the leg will occur if the patient is made to sit up in bed with extended legs and the head flexed to the chest. In cases of bilateral sciatica, the same phenomenon is manifested in both legs at once. In some (not acute) cases the movement described is not manifested, but a noticeable contraction of the musculature takes place, or a peculiar jerk of the leg occurs. This symptom reminds one greatly of the sign described by Brudzinsky in persons with cerebrospinal meningitis; in all likelihood, the genesis of this phenomenon is the same in cerebrospinal meningitis as in sciatica. It is also the same in root sciatica, except that this sign may be observed.

Apparently the second of the symptoms described is akin to the Néri [5] sign of "bowing." When the patient, in a standing posture, is made to bow, he flexes the knee on the affected side as if curtseying; simultaneously a sensation of pain appears in the leg. On the other hand, the Néri sign may be considered identical with the Lasègue sign (elicited in a standing posture), and the flexing of the leg in the knee represents an arbitrarily provoked second phase of the Lasègue sign, with the intent to weaken the strain of the nerve. The Néri sign is seen in sciatica of the trunk also, whereas the symptom described is a token of root sciatica exclusively.

CAUSATION OF SIGNS AND SYMPTOMS

What conditions the phenomena depicted? It is commonly reckoned, when explaining symptoms of pain, that they are caused by irritation of the nerve or of the nerve roots in consequence of their tension. Indeed, Deutsch [6] proved on cadavers that eliciting the Lasègue sign causes a strain of both the nerve trunk and the roots. It is this straining of the roots when the extended leg is raised that explains the almost unfailing presence of the Lasègue sign in root sciatica and in cerebrospinal meningitis. Stoffel [7] was able to demonstrate by microscopy that with the raising of the extended leg the nerve is stretched and strained, whereas with the flexion of the leg at the knee the nerve relaxes and becomes undulated, with the consequence that the roots relax correspondingly. This relaxation of the nerve and roots when the leg is flexed at the knee explains the painless second phase of Lasègue.

5. Néri, quoted from Tinel: Nouveau traité de médec., Paris, 1927, pt. 21.
6. Deutsch: Wien. klin. Wchnschr. **34**:293, 1921.
7. Stoffel: München. med. Wchnschr. **16**:1365 (June 24) 1913.

The Lasègue contralateral sign has the same origin, with this difference; the roots on the unaffected side are stretched, and this movement is transmitted to the roots on the affected side, causing pain in the affected extremity.

To explain the pains accompanying the symptom of the flexed head, it is necessary to take into consideration also the tension of the roots, which is brought on by the shifting of the spinal cord. Indeed, I have been able to prove on cadavers that enforced flexion of the head to the chest is associated with an upward motion of the spinal cord of nearly 1 cm. in the lumbar region. This shifting, entailing that of the roots also, strains and irritates them. When the legs are stretched out in a sitting posture, the roots are strained to a certain degree, and their new tension, due to flexion of the head, augments the irritation; therefore in this posture, the symptom is more conspicuously manifested. The flexion of the leg (or of both legs), which relaxes the strain of the roots, weakens the pains in the roots or even leads to their cessation. Another factor that does not fail to influence the arising of pain when the head is being flexed must also be taken into consideration, namely, the heightening of pressure in the spinal canal. In my investigations on patients during lumbar puncture, as well as on cadavers, I was able to ascertain that enforced flexion of the head heightens the pressure in the spinal canal to a marked degree. If a puncture is made in the lumbar region of a cadaver, the cerebrospinal fluid will not flow out at all, or will only ooze out by drops; if the head is flexed toward the chest, the fluid begins trickling out in a stream. Such a rise of pressure, by squeezing the roots and compressing them in the intervertebral interstices, also contributes in a certain measure to irritate the roots.

Thus it becomes evident that symptoms of pain are brought about either by irritation of the nerve roots through their straining or pressure (in nerve root sciatica) or through irritation of the nerve trunk (in trunk sciatica). Flexion of the leg at the knee and the hip, which serves to diminish the tension of the roots and of the nerve, lessens the pains and leads to their disappearance.

MECHANISM OF ORIGIN OF MOTOR PHENOMENA

What is the mechanism of origin of the motor phenomena?

Bechterew [7] considered that the Kernig sign in sciatica is of reflex origin, and that it is occasioned by the pains caused by tension of the nerve. Margulis [8] held that the Kernig sign is consequent on irritation of the vegetative fibers passing through the posterior root and the subse-

8. Margulis: Acute Infectious Diseases of the Nervous System, Moscow, 1928 (Russian).

quent heightening of muscular tonus. It would be natural to suppose, by analogy with the mechanism of the arising of symptoms of pain, that the motor phenomena are dependent on the irritation of the motor roots. It is difficult, indeed, to suppose that only the sensory part of the nerve becomes irritated in consequence of the tension of the root nerve (more particularly the funiculus, which is commonly affected in root sciatica). The motor part of the nerve becomes irritated also, and this irritation is signalized by the increased tonus in the corresponding musculature and by the Kernig sign.

The motor phenomena already recorded, however, are of complex nature: muscles innervated from different nerve trunks take part in the motion, while, on the other hand, muscles innervated by the ischiatic nerve do not take part in it. It is therefore difficult to suppose that the movements described are entirely dependent on irritation of the motor part of the lumbosacral roots.

If one analyzes, for example, the Bechterew symptom, one will see that in a sitting posture with legs outstretched (phase 1 of the Lasègue sign) the lumbosacral roots attain a maximum of tension and irritation; flexion of the leg at the knee and hip (phase 2 of the Lasègue sign) causes relaxation in the roots on the corresponding side and, in a lesser degree, also the opposite side; a more marked relaxation of the roots is attained through flexing the affected leg, and flexion of both legs gives a maximum of relaxation. In fact, an entirely painless posture is associated with the flexion of the affected extremity or of both legs. In acute cases, flexion of the unaffected leg alone is not sufficient to bring about cessation of pain, and the patient is never able completely to straighten the affected extremity; if one effects such a straightening by force (by pressure on the knee) the patient throws himself back, thus lessening the strain of the nerve trunk and roots.

In the first of the symptoms I have recorded, raising the unaffected leg conduced to the straining of the roots on the unaffected or less affected side. The flexion of the affected extremity that this elicits lessens the tension of the roots on the affected side. It is evident from the mechanism described that this symptom appears only in acute cases of root sciatica characterized by violent pain; in subacute cases the raising of the unaffected leg alone is not sufficient to provoke a painful tension and a corresponding reflex on the affected side. One finds a similar tendency to relaxation of the roots and lessening of their irritation in the motion which results from flexing the head. Thus, the phenomena recorded assume a character of expediency, based on the purpose of attaining a painless posture. The impulse for these motions is the pain which is caused by the tension and irritation of the nerve trunk and roots; it follows, therefore, that these motions must be considered as reflex, connected with pain, i. e., with irritation of the

sensory neuron. Beyond doubt, it is to these movements that those movements should be referred which are connected with irritation of the motor part of the root (and the vegetative fibers), i. e., the alteration of the tonus in the corresponding muscles.

The practical import of these phenomena is twofold. In cases characterized by subjective symptoms only, i. e., by the patient's sensations, it is permissible to seek objective signs that allow one to differentiate organic conditions from functional ones and to recognize conscious and psychogenic aggravation and also simulation (the last has frequently been observed lately with regard to sciatica). I consider the phenomena described as objective tokens.

The Kernig and Bechterew signs may be observed in both root sciatica and trunk sciatica. Concerning the rest of the motor phenomena, they are the symptoms of root sciatica exclusively. Therefore, these symptoms help to localize the process in sciatica, and this is of immense importance both for the investigation of the real origin of the disease and for the selection of the curative process and the exact site of its application.

CONCLUSIONS

1. A series of motor phenomena are to be observed in some cases of sciatica, chiefly in acute ones. Some of these phenomena are seen in trunk and root sciatica (Kernig and Bechterew signs), and some in root sciatica (symptoms of contralateral sciatica and motor symptom with flexion of the head).

2. These phenomena are of a reflex nature and are immediately connected with the pains arising from tension and irritation of the nerve and roots. Besides this, the immediate irritation of the motor part of the roots apparently plays a part in their origin.

3. As belonging to the objective symptoms of sciatica, these phenomena allow one to differentiate organic disease from functional pains and reflex neuroses sometimes following sciatica and also to recognize aggravation and simulation of the illness. Moreover, they should aid greatly in determining the precise localization of the disease.

THE SCIATIC SYNDROME*

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Ever since Cotugno described sciatica, this term has been loosely applied to any condition characterized by pain in the lower part of the back and lower limbs, regardless of the underlying cause and of the other clinical manifestations associated with the pain. One finds the term "sciatica" applied to designate such conditions as sciatic neuralgia, sciatic neuritis, sciatic radiculitis, meralgia paresthetica, lumbago, myalgia, myositis, and what not, as if all these conditions were one and the same clinical entity. As pain in the lower back and in one or both lower limbs is, in the majority of cases, merely a symptom-complex which may be present in various and different clinical entities, we would suggest that this symptom-complex be designated as the "sciatic syndrome."

Lack of knowledge of the pathology of the syndrome is most likely the cause of the existing confusion as to its clinical conception, and it remains for the clinician to formulate his conception as to the nature of the syndrome, purely on the basis of clinical observation.

Owing to the frequent appearance of the sciatic syndrome after trauma, the problem has assumed an important rôle in industrial medicine. Workmen's Compensation Boards not infrequently seek information as to the relationship of injury to the syndrome, as well as to the probable duration of the disability, in order to enable them to make adequate awards to those injured. In these cases it is also important that there prevail some uniformity of opinion as to the nature of the various clinical conditions associated with the syndrome.

It was for these reasons that we undertook this study. We had at our disposal 317 cases of this syndrome admitted to the neurologic wards of the Mount Sinai Hospital during the past ten years.

An analysis of the material permitted the following grouping:

I. Patients with paroxysmal lancinating pains in the lower part of the back and in the lumbosacral distribution without organic neurologic signs and without evidences of involvement of the osseo-arthritic structures or of their adjacent soft parts, conditions which we designate "sciatic neuralgias," three cases.

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II. Patients with more or less continuous pain in the same distribution with evidences of involvement of the osseo-arthritic structures or their adjacent soft parts. This group includes 267 cases and is subdivided into two subgroups:

a. Patients without neurologic signs of involvement of the lumbosacral roots or nerves. For the sake of convenience we designate these "the orthopedic cases."

b. Patients with objective signs pointing to involvement of the lumbosacral roots or nerves—radiculitis or neuritis.

III. Patients in whom the sciatic syndrome is an early and prominent feature of a clinical picture the underlying cause of which is a neoplastic, inflammatory, vascular or degenerative disease of the spine, pelvis, cord, meninges, roots or nerves in this area—forty-seven cases.

ANALYSIS OF CASES

GROUP I.—This group consists of three cases: one male and two female patients; two in the fourth decade of life and one in the second decade. The

A Comparison of Some Features in the Two Subdivisions of Group II

	Group II (*a*) (66 Cases)		Group II (*b*) (201 Cases)	
	Number of Cases	Per Cent	Number of Cases	Per Cent
Age incidence (same in both groups)				
Sex—Males	40	67	125	62
Females	26	39	76	37
Sudden onset	14	21	55	22
Trauma before onset	8	12	28	13
Pain in back radiating down	49	74	126	63
Gait disturbance	20	30	72	35
Spine deformity	11	16	28	14
Lasègue sign	33	50	116	57
Tender spine, sacro-iliac joint or sacrosciatic notch	40	60	145	72
Disturbance in muscle tone, volume or power	0	..	96	47
Disturbed knee reflexes	0	..	110	55
Disturbed ankle reflexes	0	..	163	81
Disturbed knee and ankle reflexes	0	..	86	42
Sensory disturbance of definite segmental or radicular distribution	0	..	109	54
Sensory disturbance vague	0	..	20	10
Paresthesias	0	..	51	46

duration of illness prior to admission was one year in two and eight months in the other. The onset was gradual in all. One of the patients had a similar attack in the same leg six years before. There was no objective evidence of disease referable to the lumbosacral nerves, or to the osseo-arthritic structures or the neighboring soft parts. The presence or absence of Valleix points is not mentioned.

The presence of paroxysmal, shooting pains in the distribution of the sciatic nerve, in the absence of evidence of organic disease of the nerve or its roots, or of the vertebral or pelvic bones or adjacent soft parts justifies our designation of these three cases as sciatic neuralgia. No etiology was ascertainable.

GROUP II, *a.*—This subgroup contains sixty-six cases: forty males and twenty-six females. The patients' ages in decades were as follows: second, one case; third, seven cases; fourth, twenty-four cases; fifth, fifteen cases; sixth, ten cases; seventh, nine cases; most of them were between 35 and 45 years of age. The occupation of forty-two necessitated standing all day.

The onset was sudden in fourteen; in eight it was preceded by trauma to the back; in three the onset was preceded by abscesses (in some remote part); in one the onset was simultaneous with an attack of cholelithiasis; two patients had been suffering from frequent "colds" and "sore throats"; three had had previous similar

attacks. Twelve had diseased teeth and five diseased tonsils; three had both. One patient had pes planus, and two had hallux valgus; in three the prostates were enlarged; two had hemorrhoids; two had arteriosclerosis; one had an inguinal hernia, and another was extremely obese.

In forty patients the pain began in the lower part of the back or in the gluteal region and radiated down the flexor surface of the thigh and leg; in twelve the pain began in the back of the thigh or knee and radiated up; in four it began in the back and radiated down the posterior surface of both thighs and legs; and in two it began in the legs and radiated up to the back. In three, the pain was aggravated by sitting. In seven, walking relieved the pain, while in the remainder it aggravated the condition.

It was impossible to classify the various types of pain as described by the patients. Pain, a wholly subjective symptom, is of little value as a diagnostic aid for the determination of the site or the nature of the pathologic process. In many patients who said that they were suffering from paroxysmal pains, observation in the wards showed that the pain was continuous with paroxysmal exacerbations.

The Laségue sign was present in thirty-three cases, in three of which it was bilateral; in five there was spasm of the erector spinae group of muscles with rigidity of the spine. One patient had kyphosis in the lumbar region and five had scoliosis.

Vertebral tenderness was present in twenty-one cases; in sixteen there was tenderness to deep pressure over the sacrosciatic notch and over the course of the sciatic nerve on the affected side. In addition to these, in one patient there was tenderness over both sacro-iliac joints, and in another over both sacrosciatic notches. In a considerable number, there was tenderness over the vertebral column, sacro-iliac synchondrosis, sacrosciatic notch and along the course of the sciatic nerve in the same case.

Twenty patients had some disturbance of gait chiefly due to attempts to spare the affected limb or to prevent jarring of the spine or pelvis, or both.

There was no objective neurologic condition in any of the patients in this group. The results of a lumbar puncture in all cases in which it was performed were negative.

Thirty-two patients in this group were subjected to x-ray examination; in eleven of these the conditions were normal; in nine there was evidence of spondylitis in the lumbosacral spine; one showed sacralization of the fifth lumbar vertebra, and another spondylolisthesis of the fifth lumbar vertebra; six showed sacro-iliac arthritis, in four of which it was bilateral; three showed pathologic processes in the hip joint; one, spondylitis of the lumbosacral vertebrae and arthritis of both sacro-iliac joints, and one showed a partially destroyed second lumbar vertebra.

The results of treatment may be summarized as follows: In nine patients rest was sufficient to relieve the pain; in thirty, rest in bed with the use of epidural injections (from one to five were given) was followed by relief of the symptoms; in three, rest in bed and baking produced the same results; in seven, rest, epidural injections and baking were necessary; in four others, rest and epidural injections gave no relief until a brace or cast had been applied. In two, rest, baking and the administration of salicylates were followed by good results; in one the application of a brace was followed by immediate relief, while in two others rest, baking and salicylates gave no relief until immobilization was resorted to; in two patients, three epidural injections did not afford any relief. One patient was relieved by injections of nonspecific protein; in another nonspecific protein and epidural injections were of no benefit until a brace was applied.

GROUP II, *b*.—This subgroup includes 201 cases. There were 125 males and 76 females. The patient's ages in decades were as follows: third, twenty-two cases; fourth, sixty-five; fifth, sixty-four; sixth, twenty-eight; seventh, nineteen; eighth, two, and ninth, one case; most of the patients were between the ages of 35 and 45 years. The occupation of 140 necessitated being on the feet all day. The condition was bilateral in three cases.

The onset was sudden in fifty-five cases, in twenty-eight of which it was preceded by trauma to the back; in one of these the trauma preceded the onset by two months, in another by five months, in another by nine months, in still another by two and one-half years; in the remaining twenty-four cases the onset immediately followed the trauma. In one woman there was a sudden onset during an infection of the upper respiratory tract following a normal labor, and in another it appeared suddenly one week after labor; in another it appeared immediately after a forceps delivery.

In six cases, the syndrome developed during an attack of "grip." Sixteen patients had had one or more previous attacks. One of these had had two previous attacks, the first thirty and the second one and one-half years before; five others had had two previous attacks within the preceding two years; one had had a previous attack fifteen years before; one, twelve years before; two, ten years before; four, three years before; one, eighteen months before; one twelve and another six months before.

One patient was subject to frequent sore throats and backaches; ten had had rheumatic pains in the limbs and polyarthritis for years; four had had frequent attacks of what was diagnosed as lumbago; four had frequent attacks of tonsillitis; four had been suffering from hay-fever for years; three were subject to attacks of cholelithiasis. In one woman, the syndrome came on simultaneously with severe leukorrhea, but the vaginal smear did not show gonococci.

Four patients were unusually obese; three had marked pes planus; four had varicose veins; five, fibroids of the uterus, which the gynecologist said was not responsible for the syndrome; six had inguinal hernia, in two of which it was bilateral; one had a femoral hernia; twelve patients were markedly neurotic. Thirteen patients had diseased teeth; sixteen, diseased tonsils, and three had both. Twenty-five had enlarged prostates, without evidence of malignancy. Thirty-five patients had albuminuria; six of these also had casts and two had pus cells, without other evidence of marked renal involvement. In eight cases, the syndrome began with disturbances in urination; these, however, were only transitory and occurred in the patients with enlarged prostates. Seven patients had marked arteriosclerosis.

In 126 cases, the pain began in the small of the back or in the gluteal region, and radiated down the flexor surface of the thigh and leg on the affected side; in twenty-six it began in the hip or thigh and radiated to the foot; in twenty-four it began in the back of the leg; in eight of these it radiated up the back of the thigh to the hip; in four it ascended only as far as the upper part of the thigh; in eight it radiated down to the foot; in two it radiated up and down; in two it began in the leg and radiated to the back; in two others it was localized to the leg and foot, in one to the ilium; in one it began in the popliteal space and radiated up and down; in two it began in the back of the thigh and radiated up and down; in two others it began in the foot and radiated to the toes and up the leg; in one it began in the thigh and radiated down and up to the gluteal region of the same side and later extended to the gluteal region of the opposite side; in one it began in the back and radiated across the buttock to the posterolateral part of the thigh as far as the ankle and on the anterior part of the thigh as far as the knee. In the remaining cases the direction of the radiation is not mentioned.

Ten patients were unable to sit on account of pain over the tuber ischii. In five, rest aggravated, and in five others, movement alleviated the pain. In the largest number of cases, however, movement increased the pain. In four it was as severe during rest as during motion; in twenty-eight, rest diminished the pain.

Fifty-one patients complained of various forms of paresthesia (burning, numbness, coldness, tingling, sensations of pins and needles and a "woody-like" feeling) in the distribution of the sciatic nerve.

The pains described by these patients did not differ from those complained of by the patients in subgroup II *a*.

The Laségue sign was positive in 116 cases on the side affected; it was present on both sides in nine, in three of which the syndrome was also bilateral. Twenty-four cases presented a compensatory scoliosis. Complete rigidity of the spine was noted in four patients. Forty-five patients had definite tenderness to percussion over the dorsolumbar spine, sacrum or coccyx; two had tenderness over the crest of the ilium; sixty-seven had sacro-iliac tenderness, in five of whom it was bilateral; thirty-three had tenderness over the sacrosciatic notch, and twenty-seven tenderness over the sciatic nerve; two had tenderness over the tuber ischii.

Ninety-six cases showed some disturbance either in tone, volume or power of the muscles supplied by one or more of the lumbosacral nerves.

The knee reflex was diminished in 108 and absent in 2 cases; the ankle reflex was diminished in 112, and absent in 51 cases. Eighty-six patients had at the same time a diminished knee reflex and a diminished or absent ankle reflex; in one patient with a diminished knee reflex, there was an exaggerated ankle reflex on the same side.

Four patients had drop foot with electrical changes in the peroneal groups on the affected side.

In 129 cases, there were evidences of objective sensory disturbances; in 100 of these they were definitely radicular in type, in 20 of which they were localized to the fifth lumbar and first sacral; in 89 the sensory disturbances were distributed in various segmental combinations beginning from the twelfth dorsal to the third sacral segment. In no case was there any involvement of the fourth or fifth sacral segments. In the remaining twenty cases, there was no question as to the presence of objective sensory disturbances, but their precise anatomic distribution could not be determined.

Lumbar puncture was performed in eighty-seven cases. The spinal fluid was normal in all except six, in which there was a pleocytosis; in one there were 80, in one 33, in one 30, in another 28; in two, 12, and in two others 10 cells to the cubic millimeter. The cells were all lymphocytes. In three of these there was also marked increase in the spinal fluid pressure. The globulin content was normal and there was no evidence of block or of the Froin syndrome in any of these cases.

X-ray examination was made in ninety-two cases. The observations are recorded as follows: Mild hypertrophic spondylitis of the lumbar vertebrae and both sacro-iliac joints in five cases; spondylitis of the lumbosacral vertebrae in twenty-two cases; arthritis of the sacro-iliac joint in fifteen cases; spondylitis of the lumbar vertebrae and sacro-iliac arthritis in the same patient in twenty-two cases; arthritis of the hip joint in two cases; absorption of the body of the fifth lumbar vertebra, and condensation of the ischiopubic portion of both ossa innominata and of one femur in a man, aged 67; senile atrophy of the fifth lumbar vertebra in one; sacralization of the fifth lumbar vertebra in two cases; displacement of the coccyx in one. In seventeen of the ninety-two cases, the x-ray examination

gave negative results. There was no apparent relationship between the severity of the symptoms and the x-ray observations.

The results of treatment of the patients in this group may be summarized as follows: All patients were kept in bed at absolute rest. This was sufficient to alleviate the pain in thirty-five cases; in twelve it was also necessary to resort to baking and diathermy; in 114, rest and from one to five epidural injections were given; in eleven baking was added to the rest and epidural injections; in four, epidural injections and diathermy were given; in fourteen it was necessary to resort to epidural injections, physiotherapy and to the application of a brace or cast before the patients were relieved; in four others nonspecific protein injections were given in addition to the epidural injections; one was relieved by the injection of alcohol into the external cutaneous nerve. Two patients were subjected to exploratory laminectomy, but a tumor was not found. One of these was discharged with the condition unchanged, and the other was subjected to another operation during which the sciatic nerve on the affected side was exposed; the surgeon reported the nerve to be unusually red, but nothing further was done until the wound healed; under deep x-ray therapy there was complete relief of the symptoms although there was no change in the objective neurologic signs. One woman, aged 28, without clinical or serologic evidence of syphilis, was subjected to all of the mentioned methods of treatment, but was not relieved until she was given a vigorous course of antisyphilitic treatment. Six patients left the hospital before any treatment was instituted; in eleven cases the results of treatment are not mentioned. Three patients in this group had active diabetes and three others had syphilis; the syndrome in these patients was unilateral and yielded to the ordinary methods of treatment.

Group III.—This group consists of forty-seven cases in which the sciatic syndrome was an important, and in most instances, an early feature of the clinical picture. The group contains one case of sarcoma of the ilium (necropsy); one of carcinoma of the ilium (x-ray); three degenerative diseases of the cord (two proved by operation and one still under observation); one metastatic carcinoma of the lumbar vertebrae; one hypernephroma of the cord at the tenth dorsal segment (operation); one metastatic carcinoma of the hip, head and neck of the femur (x-ray); one melanosarcomatosis with involvement of the dorsolumbar spine and pelvis; eight neoplasms of the cord (one at the eighth to the eleventh dorsal; two at the tenth to the twelfth dorsal; one at the first to third dorsal; one at the sixth and seventh dorsal; one of the second dorsal; one at the first dorsal, and one at the first lumbar segment) all proved by operation; one osteochrondroma of the lumbar spine (operation); nine tumors of the cauda equina (operation); one neuritis of the cauda equina (operation); two gliosis of the dorsolumbar cord; one inflammatory disease of the cord (operation); two patients with hemorrhage about the cauda equina; five Pott's disease of the dorsolumbar vertebrae; three spina bifida occulta and two infectious radiculomyelitis of the lumbar cord. One case existed with a tuberculous hip; one with fracture of the lumbar vertebrae; and one with varicosities of the cord. For the purposes of this study it is not necessary to enter into a more detailed analysis of this group.

COMMENT

Group I.—The Neuralgias: The cases in this group were characterized by the paroxysmal appearances of the pain and its shooting character, with comparative freedom from pain between the paroxysms. On admission, and throughout the patients' residences in the hospital

there was no objective evidence of involvement of the nervous system, or of the osteo-arthritic structures or contiguous soft parts.

With our present conception of the neuralgias we may be justified in designating these cases as "sciatic neuralgia." In doing so, however, we wish to quote Oppenheim, who in discussing sciatic neuralgia comments on the great difficulty of differentiating sciatic neuralgia from sciatic neuritis. "In a great majority of cases," he said, "the signs of neuritis are absent, but there is no doubt that all stages of transition between neuralgia and typical neuritis do occur." Klug regarded all cases of so-called sciatica as a perineuritis; Gowers, Müller, Edinger, Fritz Kraus and others were of the same opinion.

The occurrence of only 3 cases of this type in a series of 317 cases is noteworthy; it harmonizes well with the frequency of occurrence of neuralgia in other nerves, as encountered in ordinary neurologic practice. At this point it may perhaps be emphasized that the diagnosis of sciatic neuralgia should be made only after prolonged observation. Some of our cases of neoplasm of the lower cord, cauda equina and of other diseases of the lower spine and pelvis began with the typical clinical picture of what is usually designated as sciatic neuralgia.

Group II, a.—This group, designated by us as "the orthopedic group," contains sixty-six cases. Every patient in this group complained of pains in the lower part of the back or the buttock, radiating down the thigh, mostly along its flexor surface. Except for the absence of neurologic signs, there was nothing in the clinical history or in the course of the disease that would distinguish these cases from those with neurologic signs. We would attribute the pain in these cases to the effects of irritation of the lumbosacral roots or nerves by edema or inflammatory process in the osseo-arthritic structures or in the adjacent soft parts or in both. The absence of neurologic signs may perhaps be due to the fact that the pathologic process in the bones, joints and soft parts is not sufficiently intense to interfere with the conductivity of the nerves. This hypothesis is substantiated by the clinical fact that when these patients are seen early and are subjected to rest in bed and proper treatment, they rarely go on to the production of neurologic signs of involvement of the nerve or root. These patients, however, require repeated neurologic examination for the possible appearance of neurologic signs, which would then place them in the succeeding subgroup, or what may be more serious, in the group of cases in which the sciatic syndrome is secondary to a neoplasm of the cord, roots or meninges, or of the osseo-arthritic structures and their adjacent soft parts in this region.

Group II, b.—This group contains by far the greatest number of cases. The location and radiation as well as the nature of the pain was

the same as in the patients in the preceding group. All, however, showed objective evidences of involvement of the lumbosacral roots or nerves. The latter was manifested by disturbances either in power, volume or tone of the muscles in the gluteal region or in the lower extremity on the affected side, or by changes in the deep reflexes or in sensation, or in all of these.

The diminution of muscle power was never striking; not infrequently it was difficult to determine whether it was actual, or only apparent and due to the patient's reluctance to move the painful limb. The diminution of the volume of the muscle, when present, could be evaluated much more readily than the weakness. The differences in volume between the affected and healthy limbs varied from ½ to 2 inches (1.27 to 5 cm.). The diminution in tone of the involved muscles was usually in proportion to the diminution in volume. There were, however, some cases of diminished tone but without diminution in volume as determined by measurements. In nine cases in which the disturbances in the volume and tone of the muscle were sufficient to warrant electrical examination, the responses were normal in six; in the remaining three the involved muscles showed only slight quantitative changes. We were apparently not dealing with an advanced degenerative process. Only five patients showed fibrillary twitchings in the involved musculature.

The large number of patients with disturbances of the knee and achilles reflexes seems to us of great significance, especially if we take into consideration the disturbances of both the knee and achilles reflexes in the same patient, as well as their association with objective sensory disturbances conforming to the radicular type of distribution in the very segments in which the reflex arcs for these reflexes are situated. This would seem to indicate that in these cases there is a more widespread involvement of the nerve. Here one is apparently dealing with an involvement of the lumbosacral roots, or nerves—a radiculitis or neuritis. The beginning of the pain in a large majority of cases in the lower lumbar region, and its early radiation toward the gluteal region, would seem to point to an early involvement of the rami posteriores of the lumbosacral nerves, some of which perforate the gluteus maximus to supply this region with cutaneous sensibility.

Except in a few cases in which there was slight lymphocytosis in the spinal fluid, there was no reason to believe that the involvement of the roots had occurred before their exit from the vertebral canal. The fine differentiation, elaborated by Sicard and Foix as to radiculitis, docitis and funiculitis, based on observations of the spinal fluid, was not borne out by our cases. Putti, who has recently interested himself in this subject, was also unable to confirm Sicard's claims.

The Laségue sign was positive in 116 cases. According to Helweg, this sign is not necessarily evidence of involvement of the sciatic nerve, because in his experience the sign may be due to a strain of the muscles themselves. This is corroborated by Warburg and others. We doubt whether one is justified in regarding the Laségue sign as pathognomonic of involvement of the nerve. In our series a positive Laségue sign was just as common in the patients without as in those with neurologic signs.

Neither evidences of involvement of the sympathetic nerve, nor unusual vasomotor or trophic disturbances were noted in any of our cases.

It is noteworthy that so many patients in this as well as in the preceding group showed some objective evidences of the involvement of the osseo-arthritic structures or of the adjacent soft parts in the affected areas. Such involvement was manifested either (1) in disturbances of gait during which the affected limb was spared as much as possible; (2) in rigidity of the spine, especially of the lumbosacral portion, with or without muscle spasm; (3) in homologous or heterologous scoliosis (in the more chronic cases); (4) in pain on lateral compression of the iliac crests (Erichsen's sign); (5) in tenderness to deep pressure over the dorsolumbar spine, sacrum, gluteal region, sacroiliac joints and sacrosciatic notches; (6) in visible discomfort and fatigue during continued effort in standing, walking or changing of position, with aggravation of the pain during sneezing, coughing and straining, or (7) in a poorly developed gluteal fold on the affected side.

In most of the cases the involvement of the osseo-arthritic structures, as manifested by some or all of the aforementioned criteria, was confirmed by x-ray examination. In just as many cases, however, the diagnosis of involvement of these structures and their contiguous soft parts could be established by inspection, palpation and percussion. In this connection we wish to point out that, except perhaps in neoplasms of the bone, or in such rare cases as sacralization of the fifth lumbar vertebra, or in spondylolisthesis, x-ray examination is not of as much value as is usually attributed to it. Routine x-ray examinations of persons after the third decade of life show in a large number some evidences of osseo-arthritic changes in either the spine or the pelvis, although these subjects have no complaint referable to these structures. Furthermore, many of our cases showed x-ray evidences of involvement of both sacro-iliac joints, although the sciatic syndrome was present on one side only. As a matter of fact, spondylitis when clearly marked on the screen is a later stage of this condition. The degree of involvement of the osseo-arthritic structures, as interpreted by the radiographer on the plates, did not bear a definite relationship to the severity of the clinical picture. Obviously, pathologic processes in the soft parts, other

than actual calcification or ossification (none of which could be demonstrated in any of our cases) cannot ordinarily be visualized by x-ray examination.

Many Continental and American observers lay great stress on bony deformities and arthritic changes in the lumbar spine and sacro-iliac articulations as pathogenetic factors in the sciatic syndrome. If this were so, one would expect the incidence of the syndrome in persons with such bony and joint changes to be much larger than it actually is. Such a theory would not explain the disappearance of the subjective symptoms, and, in some cases, even of the neurologic signs during a persistence of the bony and joint changes. There must be a superadded factor such as trauma to the soft parts or infection somewhere in the body, removal of which affects the syndrome favorably although the osteo-arthritic changes persist.

We are inclined to believe that in most of these cases it is within the soft tissues (ligaments, muscles, fascia, tendons, etc.) in the affected region that the pathologic basis for this syndrome must be sought. A review of the mode of onset in many cases showed that the symptoms followed trauma to the lower back. In some of these the onset was so sudden that it would not be unreasonable to believe that hemorrhage into or a laceration of the soft parts with subsequent edema had occurred. We can readily conceive that such swelling in the soft parts may also affect the adjacent nerve roots or trunks giving rise to the neurologic component of the syndrome. Inflammatory processes associated with infections may similarly involve the soft parts and even the osseo-arthritic structures. Injuries to muscles, fascia, ligaments and synovial membranes are notoriously slow in healing; they are seldom given enough rest and time; patients with such injuries are put to work too early and moderate effort then becomes a relative strain, far greater than these structures can bear; hence the chronicity of these cases. Trauma to or infections in these parts may run their course with little or no demonstrable evidence of involvement of the adjacent nerve structures, as illustrated by the large number of these cases that run their entire clinical course without ever giving objective evidences of involvement of the nerve. The importance of taking all this into consideration in cases in which the sciatic syndrome follows trauma, especially in workmen's compensation cases, is self evident.

In support of this conception of the pathogenesis of the syndrome, we may also offer our observations as to the results of therapy. In many patients mere rest in bed was sufficient to relieve the pain; in others, rest in bed and the administration of antirheumatic remedies were necessary to obtain a similar result; in most of them, however, it was necessary to resort to epidural injections. Depending on the severity and chronicity of the case, from one to five injections were

necessary. We cannot find a satisfactory anatomic or physiologic explanation for the undoubted beneficial results following these injections. Some of the patients had to be given physiotherapy in the form of baking or diathermy in addition to rest in bed and epidural injections. In passing, we may mention that in every case, foci of infection were sought, and, whenever found, eradicated; the beneficial effects following these procedures were in some cases striking. In the absence of constitutional symptoms in almost all of our patients, it was difficult to keep some of them continuously in bed—a therapeutic measure to which we attach the greatest importance. These patients, as well as in the more chronic cases, obtained no relief until some form of immobilization, such as a plaster of paris cast or brace was applied. Whenever the latter was indicated we always insisted that it be worn for months, otherwise the relief would be transient and incomplete. Both on discharge and in the "follow-up" clinic we found that whereas the subjective complaints and such signs as disturbances of gait, scoliosis and local tenderness over the spine, joints and soft parts had disappeared, the neurologic signs, except perhaps the objective sensory disturbances, persisted, some of them remaining permanently. Obviously, the osseoarthritic changes demonstrable on the screen remained unaffected.

Group III.—This group contains forty-seven cases. All patients in this group had at one time or other, in the course of their disease, a sciatic syndrome. In most of them, however, the syndrome was associated very early with some features indicating that one was not dealing with an ordinary case of lumbosacral radiculitis, neuritis or neuralgia. The early onset of bilaterality of nerve involvement was striking; in only six cases in this entire group did the sciatic syndrome remain unilateral throughout the disease. Owing to bilaterality of involvement, disturbance in sphincteric control was an early and prominent symptom. The relatively rare occurrence of this symptom in the other groups was an important differential criterion. The objective neurologic disturbances were also more constant and more definite, especially the objective sensory disturbances. The root phenomena usually associated with extramedullary neoplasms were typical. The nature of the pain and its radiation was similar to that in the other groups, except that in the cases in which the neoplasm involved the bones and meninges the pain was much more severe and more continuous. Paresthesias were also more common and more severe. Sensory disturbances in the sacrococcygeal distribution were also much more common in this group.

A detailed discussion of the cases in this group is not within the scope of this paper. We may mention, however, that here we were greatly aided by manometric studies of the spinal fluid for the purpose

of determining partial or complete block, as well as by the examination of the fluid for xanthochromia and for other evidences of the Froin syndrome. In many cases, however, the precise localization of the lesion remained in doubt until we resorted to injections of iodized oil 40 per cent.

The frequency of x-ray observations indicating spondylitis and sacro-iliac disease in this group was noteworthy. This is stressed because in some of the cases these observations were regarded, prior to admission to the hospital, as sufficient to account for the syndrome, when, as a matter of fact, they were merely coincidental and had nothing to do with the patients' difficulties. It is well to bear in mind that even in the presence of negative x-ray observations a history of persistent backache with or without other evidences of the sciatic syndrome in a person who had had a previous operation for the removal of a malignant growth in any part of the body (breast, prostate, etc.) should put one on guard lest he may be dealing with a metastasis of the bone. The same is true in the presence of signs and symptoms of tuberculous infection.

CONCLUSIONS

1. The term "sciatica," as it is generally employed, is misleading. It tends to direct attention away from the most common and remediable underlying cause of the various clinical conditions characterized by pains in the lower part of the back and limbs. The use of this term should therefore be discontinued, and an effort be made to determine the underlying cause and to designate the condition accordingly, and as being associated with the sciatic syndrome.

2. In the absence of a polyneuritis or polyradiculitis from whatever cause (toxic, infectious, metabolic, constitutional, vascular, etc.), a primary mononeuritis or radiculitis of the sciatic nerve is extremely rare. In practically all our cases the sciatic syndrome was secondary to some pathologic process in the osseo-arthritic structures or their contiguous soft parts in the region under discussion.

3. Cases in which the patients have paroxysmal attacks of lancinating or shooting pains in the lower part of the back and in the lumbosacral distribution without objective evidences of involvement of the lumbosacral roots or nerves, or of the osseo-arthritic structures or their adjacent soft parts (muscles, tendons, fascia, etc.) in this region should be designated as "sciatic neuralgia." The presence of only three such cases in a series of 317 indicates the rarity of this condition, notwithstanding that most authors emphasize its frequency and employ the term "sciatica" as if it were synonymous with "sciatic neuralgia."

4. By far the largest number of patients presenting the sciatic syndrome show demonstrable evidences of involvement of the osseo-

arthritic system or of the contiguous soft parts in this region. This group may be subdivided into two subgroups: (*a*) Cases without demonstrable signs of organic nervous disease. In the absence of such signs, these cases present an orthopedic problem and we would, for the sake of convenience, designate them as "orthopedic cases." We would also emphasize the importance of early and proper treatment of these patients lest the pathologic process in the osseo-arthritic system and the adjacent soft parts become more advanced and involve the nerve roots or nerves themselves in this region. (*b*) Cases with demonstrable evidences of involvement of the lumbosacral roots or nerves. Depending on the nature and distribution of the involvement of the nerve we would designate these as cases of lumbar, lumbosacral or sacral radiculitis or neuritis. This subgroup includes 64 per cent of our entire material.

5. There are a certain number of cases in which the sciatic syndrome may appear as an early and prominent feature of a clinical picture the underlying cause of which is a neoplasm of the spine, pelvis, cord, meninges or roots. The fallacy of designating these cases as "sciatica" is self evident.

6. Except in such rare cases as sacralization of the fifth lumbar vertebra, calcification or ossification of the soft parts, or in primary or metastatic, neoplastic, or tuberculous processes in the spine or pelvis, positive x-ray observations of spondylitis or arthritis are not conclusive as to the etiologic relationship of these observations to the sciatic syndrome.

ABSTRACT OF DISCUSSION

Dr. S. E. Jelliffe, New York: It seemed to me that the discussion lacked pertinency in that the name of a thing is more or less insignificant; so long as one calls these phenomena "syndromes," "sciaticas" or "neuritides" or "neuralgias," we get nowhere. The idea should be focused on "Why is it what it is?" and not the question of "What is it?" What it is does not amount to anything. The question of "why it is" amounts to everything. The accent should be placed rightly on the etiologic factors, by the readers of the paper, it seems to me.

In listening to the paper, I was struck with the constant reiteration of "no objective neurologic disturbances were present." In view of these statements I would ask you to fantasy that our present methods in neurology of objective sensory discrimination will undergo considerable development in the near future. Some of you may remember that on the first day of this meeting when Dr. Tilney's paper was discussed, he spoke of the capacity of Helen Keller, blind and deaf, to smell the facts that while out riding they were passing through the forests or through the open fields, or going by a printing plant, etc. Also, in his description, he said that tactile examinations, auditory examination and other kinds of examinations proved that there were no objective observations, and yet here were a series of objective observations on the part of a person who could do what very few of us can do. A few people can tell just exactly what province a certain cigar was

made in, exactly where a certain wine was grown and even the vintage, but such illustrations of capacities for developing receptor discriminations are extremely rare in practice. They are not, however, at all rare for anybody who wants to take the trouble to develop them. In other words, what the burden of my phrases may attempt to convey is that newer and better methods of objective examination of the receptor capacities are desirable.

I have already indicated, just as an illustration, that in the eiditic methods of examining, various forms of receptor capacity were coming into use and were showing that great advances would be made in discrimination of the sensory mechanisms of the human body. That is only one form in which my fantasy says that we shall cease to say there were no objective observations in the future, if we know how to look for objective observations by other methods much more refined than those which are presently in use.

As a final "demented form of suggestion" for such types of examination I may mention the dream. The dream is an exquisite discriminative finder of organic syndromes, if anybody knows how to use it. I shall close, with what attitude of fantasy you may place on it, with the following fragment of a case history: I had had a wife under observation for some time. The husband had psychic impotency. The wife, in years gone by, had had two miscarriages, more or less self-induced. Finally, she came to me with the following dream: "I am packing my trunk. It is full; I lock it. I put a brown band strap around it. My husband comes and knocks at the door, and I tell him, 'You go away!'" In fun, as well as in earnest, I said to her, "You are pregnant." She replied, "Nonsense." I said, "You are pregnant. Let's mark down the day and see." At any rate, let us find out how the husband has been behaving of late. As I told you, he was a patient of mine and I had not seen him for a short time. At any rate, three or four days before the dream had occurred, successful intercourse had taken place. Two hundred and eighty days after that day a boy was born. Thus, my prediction came true. The dream had been an objective tester of reality that no Abderhalden test could rival.

The only justification I have for telling this story is this: The uterus knows more about what is going on inside of us than we do. It is a part of that "wisdom of the body" that we are constantly forgetting.

Dr. C. H. Frazier, Philadelphia: If I may be allowed to reminisce with Dr. Jelliffe, I remember that thirty years or more ago stretching the sciatic nerve used to be a popular procedure in the surgical clinic. I thought it had long been abandoned and forgotten until a few days ago a patient was brought to me with complete motor and sensory lesion of the sciatic nerve because of a vigorous attempt at relief by stretching.

Dr. Keschner: We have the same feeling that Dr. Jelliffe has. We believe that with more precise methods we would have found some objective observations even in the sixty-six cases that we labelled "without neurologic disturbances."

As to stretching the sciatic nerve, we have looked over the surgical records at the Mt. Sinai Hospital and we were unable to find a single record of stretching the nerve in the last twenty years.

SOME OBSERVATIONS ON THE LEUKOCYTE COUNT IN EPILEPSY*

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The leukocyte count in epilepsy has been discussed by a number of authors, but their opinions on this subject, as encountered in the literature, are controversial. Spangler [1] and Wuth [2] stated that before the convulsion the white cell count is normal; Riebes [3] described a leukocytosis occuring at this time, and Hartmann [4] and Di Gaspero [5] claimed that leukopenia occurs. Schultz,[6] Itten,[7] Zimmermann,[8] and Gorrieri [9] reported a lymphocytosis preceding the attack; Gorrieri [9] also postulated eosinophilia. During the seizure, Wuth [2] and Goedicke [10] found leukocytosis, Di Gaspero [5] recorded leukopenia, and Zimmermann,[8] Schultz [6] and Rhode [11] asserted that there is lymphocytosis. Zimmermann [8] and Schultz [6] proclaimed, in addition, eosinophilia. After the paroxysm, Spangler,[1] Wuth,[2] Itten,[7] Riebes,[3] and Schultz [6] observed leukocytosis, while Riebes [3] likewise noted lymphocytosis, and Gorrieri,[9] Di Gaspero [5] and Schultz [6] encountered eosinophilia. Pearce and Boston [12] and one of us (H. A. P.) [13] also mentioned the occurrence of leukocytosis in this condition, but did not attempt to relate the blood picture to the seizure.

In discussing the total white cell count, there are certain physiologic considerations of which cognizance must always be taken. There is,

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1. Spangler: Blood Findings in Epilepsy, Lancet **1**:910, 1916.
2. Wuth: Blood Changes in Convulsions, Especially in Epilepsy, Bull. Johns Hopkins Hosp. **38**:407, 1926.
3. Riebes: Ztschr. f. Psychiat. **70**:283, 1913.
4. Hartmann, cited in Lewandowsky, M.: Die Hysterie, Berlin, Julius Springer, 1914.
5. Di Gaspero: Arch. f. Psychiat. **59**:1118, 1918.
6. Schultz: Dissertation, Göttingen, 1906.
7. Itten: Ztschr. f. d. ges. Neurol. u. Psychiat. **24**:341 and 339, 1914.
8. Zimmermann: Ztschr. f. d. ges. Neurol. u. Psychiat., 1915, vol. 28; **34**:354, 1916.
9. Gorrieri: Ztschr. f. d. ges. Neurol. u. Psychiat. **15**:443, 1913.
10. Goedicke, quoted by Wuth: Bull. Johns Hopkins Hosp. **38**:389, 1926.
11. Rhode: Deutsches Arch. f. klin. Med. **95**:148, 1908.
12. Pearce and Boston: The Blood in Epilepsy: Experiments on Animals, Am. J. Insanity **60**:601, 1904.
13. Patterson: Haematological Pictures in Endocrine Syndromes Found Associated with Epilepsy, Am. J. Psychiat. **2**:429, 1923.

first, a normal or physiologic leukocytosis in which the count usually ranges from 9,000 to 14,000 per cubic millimeter. It may occur during digestion and after cold baths,[14] after strenuous exercise,[15] with brief exposure to atmospheric cold, in menstruation, in pregnancy and in the new-born.[16] The increase in leukocytes in these conditions is not limited to the neutrophils. Lymphocytes are likewise increased, most markedly in the new-born. Todd[17] stated that in view of the leukocytosis of digestion, which usually increases the number of the leukocytes by about 30 per cent, the hour at which a leukocytic count is made should always be recorded. The leukocytosis of digestion is most marked from three to five hours after a hearty meal rich in protein, especially when such a meal follows a long fast. It is absent in pregnancy and when leukocytosis from any other cause exists.

In the selection of our material, care was taken to rule out the effect of these physiologic features. All patients chosen were males. Counts were not taken immediately after a patient had had a cold bath or had engaged in excessive exercise. Nor were they made in cases in which some concomitant disease, such as tuberculosis, might tend to influence the existing blood picture. The influence of meals was taken into consideration, as will be shown in the accompanying table. Moreover, the counts were all taken in the summer to avoid any possible effects of extreme cold.

In 182 cases of epilepsy studied, approximately 50 per cent showed an increase over the normal in the total white cell count, while in 20 per cent the count fell below normal. In obtaining the white cell counts the usual technic was followed except that we employed acetic acid solutions varying in concentration from 2 to 4.5 per cent, most of which were stronger than the solutions in general use as diluents. This modification produced a clearer picture, since the other solid elements of the blood were more quickly and more completely destroyed without apparent injury to the leukocytes themselves than in the customary method.

The distribution of the total leukocytic count is indicated in table 1. For the preparation of this table, we considered the normal range as from 6,000 to 9,000 white cells per cubic millimeter. The cases studied were then divided into three groups and the average white cell count for each group was computed.

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14. Todd: Clinical Diagnosis by Laboratory Methods, Philadelphia, W. B. Saunders Company, 1923, p. 275.

15. Macleod: Physiology and Biochemistry in Modern Medicine, St. Louis, C. V. Mosby Company, p. 97.

16. Da Costa: Clinical Hematology, Philadelphia, P. Blakiston's Sons & Company, 1901, p. 178.

17. Todd: Clinical Diagnosis by Laboratory Methods, Philadelphia, W. B. Saunders Company, 1923, p. 276.

In our observations, part of which have already been published,[18] we found the increase in leukocytes in this condition to be due to an excess of lymphocytes rather than of neutrophils. It is therefore a lymphocytic leukocytosis or a lymphocytosis that we have noted. The wide variability in the leukocytic count disclosed by the preceding tabulation and a similar inconstancy observed in the differential count, not as yet reported, when taken in consideration with the relatively few cases described by some of the authors mentioned, may perhaps account for the wide divergence of opinions recorded in the literature.

The relation of meals to the total white cell count in epilepsy is shown in table 2. It illustrates the leukocyte count from three to five hours after the ingestion of food—when, Todd [14] claimed, the influence of digestive processes on the blood is most marked—in contrast with the enumeration obtained at other times.

TABLE 1.—*The Total White Cell Count in Epilepsy*

Group	Average White Cell Count	Number of Cases	Percentage
Leukopenia	4,535	37	20.3
Normal	7,660	50	27.5
Leukocytosis	13,912	95	52.1

TABLE 2.—*The Influence of Meals on the White Cell Count in Epilepsy*

Hours After Meal	Number of Cases	Average White Cell Count	Number of Cases	Average Hemoglobin Content
3 to 5	49	12,149	48	79%
1 to 3 and 5 plus	51	10,551	48	78%
Leukocytosis (?) of digestion	..	1,598	..	....

In this and subsequent tables, estimations of hemoglobin content were included to indicate that the white cell count may, theoretically at least, be affected by the secondary anemia which often appears in epilepsy. That this is not actually the case is inferred from the fact that the leukocyte rise with secondary anemia is neutrophilic,[18] whereas the increase here, as already mentioned, is lymphocytic.

Scrutiny of table 2 indicates that while there is a moderate rise in the number of leukocytes in the blood in epilepsy at the height of digestion, this tends on the average to fall within the limits of normal physiologic variation and does not appear to be directly influenced by meals. Such results are in distinct conformity with Todd's statement previously cited [17] that there is no increase in the white cell count in digestion in the presence of an already existing leukocytosis. Moreover,

18. Patterson and Weingrow: Some Observations in Connection with Epilepsy and Some of the Diseases of Childhood, New York State J. Med. **28**:1106 (Sept. 15) 1928.

the increase in leukocytosis accompanying digestion is usually neutrophilic [16] whereas in this condition it is lymphocytic. From their own statement, it would appear that the observations of Pearce and Boston [12] were made from three to four hours after a limited meal in all cases, but since an increase in leukocytosis does not appear with digestion in epilepsy this does not invalidate their conclusions.

Wuth studied five instances of a convulsive disorder of the idiopathic variety and an equal number of the nonidiopathic type but did not explicitly contrast the two. We have made a comparison of these two classes in table 3. By the term idiopathic, we refer to those instances of epilepsy without any definite evidence of a pathologic condition that might reasonably be regarded as a cause of the epilepsy; conversely, by

TABLE 3.—*The White Cell Count in Essential and Nonessential Epilepsy*

	Average White Cell Count	Number of Cases	Average Hemoglobin Content	Number of Cases
Idiopathic	10,890	125	78%	76
Nonidiopathic	11,522	44	80%	40

TABLE 4.—*The Remote Effect of Seizures on the White Cell Count in Epilepsy*

	Idiopathic Epilepsy			Nonidiopathic Epilepsy				
	Observations on Patients Without Seizures Within 4 Days Before or After Examination	Observations on Patients with Seizures Within 4 Days Before or After Examination		Observations on Patients Without Seizures Within 4 Days Before or After Examination	Observations on Patients with Seizures Within 4 Days Before or After Examination		Weighted Average	Total Number of Cases
		Grand Mal	Petit Mal		Grand Mal	Petit Mal		
Average white cell count.	10,682	12,416	10,670	12,063	10,788	10,009	11,420	...
Number of cases.....	64	55	19	30	11	4	.....	183
Average hemoglobin content	75%	72%	71%	77%	70%	70%	73.7%	...
Number of cases.....	55	45	16	30	9	3	.....	158

nonidiopathic we mean those instances of epilepsy that can probably be attributed to a definite pathologic cause, such as trauma.

Table 3 discloses the fact that the white cell count, although above normal, is practically identical in these two kinds of epilepsy within the limits of physiologic variation. It seems, therefore, that the leukocytosis frequently encountered in epilepsy is not due to the disease per se, but to some concomitant phenomenon, as Wuth has intimated.

It is generally conceded in the literature that there is a rise in the white cell count immediately before a convulsion. In table 4 the more remote effect of seizures on the white cell count is considered. Here the dichotomy of the idiopathic and the nonidiopathic classification has been preserved. Both grand mal and petit mal attacks are included and a weighted average is presented for the sake of greater accuracy, since the number of cases studied is variable.

In table 4 it may be seen that, within the limits of physiologic variation, the leukocytosis occurring in association with an attack of the grand mal type is similar in degree to that occurring in association with an attack of the petit mal type; in other words, that the seizures do not exert any remote effect on the white cell counts in either branch of the dichotomy. It might be added in passing that in the compilation of the table it was noted, in the process of selecting individuals for the group that should include only patients having seizures within four days before

TABLE 5.—*The Relation Between the Onset and Duration and the White Cell Count in Epilepsy*

ONSET	1-10 Yrs.	11-20 Yrs.	21-30 Yrs.	31-40 Yrs.	41-50 Yrs.	51-60 Yrs.	61-70 Yrs.	Average	Total Number of Cases
Idiopathic									
Average white cell count	11,552	10,313	11,762	11,125	.....	13,932	.....	11,737	...
Number of cases	54	44	10	6	0	1	0	.....	115
Average hemoglobin content	74%	72%	76%	72%	.....	90%	.....	76.8%	...
Number of cases.	23	41	9	5	.....	1	.....	.....	79
Nonidiopathic									
Average white cell count	11,508	11,646	.....	11,605	11,080	.....	9,905	.....	...
Number of cases..	21	15	.....	2	1	.....	2	.....	41
Average hemoglobin content	73%	78%	.....	70%	65%	.....	88%	.....	...
Number of cases..	20	14	.....	2	1	.....	2	.....	39
DURATION									
Idiopathic									
Average white cell count	11,691	11,669	11,366	9,728	.....	.....	.....	11,113	...
Number of cases..	34	30	18	16	.....	.....	.....	.....	98
Average hemoglobin content	75%	80%	68.4%	71%	.....	.....	.....	73.5%	...
Number of cases..	28	20	16	14	.....	.....	.....	.....	84
Nonidiopathic									
Average white cell count	11,152	12,610	12,320	11,347	.....	.....	.....	11,857	...
Number of cases..	9	16	4	5	.....	.....	.....	.....	34
Average hemoglobin content.	75%	82%	69%	73%	.....	.....	.....	74.8%	...
Number of cases..	9	16	4	4	.....	.....	.....	.....	33

or after the examination, that attacks occurring at a much briefer interval before or after the convulsion, within two or three days, for example, did not exert any influence on the leukocyte count. These observations also tend to substantiate the deduction that the leukocytosis frequently seen in epilepsy is not due to the disease per se but to some concomitant phenomenon.

In the course of our investigations, we studied the relationship of the aura to the white cell count and learned, as we had anticipated, that a connection between the leukocyte count and the presence or absence of an aura apparently does not exist.

Table 5 expresses the relation between onset and duration of the epilepsy and the white cell count in this condition. Both onset and

duration are classified according to decades and the division into idiopathic and nonidiopathic classes has been retained.

From table 5 it is evident that neither onset nor duration alters the white cell count in either variety of epilepsy.

SUMMARY AND CONCLUSIONS

1. There is considerable diversity of opinion among various authors on the subject of the blood picture in epilepsy.

2. In our observations, the total white cell count in epilepsy is widely variable: 52 per cent of the cases showed leukocytosis; 25.5 per cent gave normal counts, and 20.3 per cent showed leukopenia.

3. The inconstancy of the blood picture in epilepsy, together with the relatively few cases on which frequently the conclusions previously reported are based, perhaps accounts for the conflict of opinions in the literature.

4. The leukocytosis observed in our investigation was not neutrophilic but lymphocytic.

5. In our cases definite evidence of epileptic leukocytosis being influenced by digestion of food was lacking.

6. Within the limits of physiologic variation, the rise in the leukocyte count is the same in nonidiopathic as in idiopathic epilepsy.

7. A remote effect is not produced by either grand or petit mal seizures on the white cell count in both idiopathic and nonidiopathic epilepsy.

8. It seems that the leukocytosis frequently encountered in epilepsy is not due to the disease per se, but to some concomitant phenomenon.

9. A connection between the leukocyte count in epilepsy and the presence or absence of an aura apparently does not exist.

10. Our observations failed to show any relation between onset and duration and the white cell count in epilepsy.

11. The leukocyte count in epilepsy does not appear to be affected by the secondary anemia which often accompanies this condition.

Clinical and Occasional Notes

SUBACUTE ENDOCARDITIS SIMULATING MENINGITIS*

JOSEPHUS T. ULLOM, M.D., PHILADELPHIA

Frank emboli of the brain are not uncommon in endocarditis of the acute or subacute variety and are usually manifest by hemiplegia, monoplegia or paralysis of a cranial nerve, but emboli producing symptoms of meningitis have only rarely been reported. In an article on subacute endocarditis, Osler[1] spoke of cases showing predominant meningeal symptoms but did not go into detail. My purpose in this paper is to record a case in which, as a complication of a subacute endocarditis, an accompanying meningitis occurred. Such complications are rare, yet they probably occur much more frequently than would seem to be the case, for in many such instances the usual diagnosis made is that of encephalitis.

REPORTS OF CASES IN THE LITERATURE

P. Lereboullet and J. Mouzon reported[2] a case of subacute endocarditis or, as the French call it, prolonged infectious endocarditis, which showed meningeal symptoms. Their patient had severe headache, photophobia and a transitory left hemiplegia; the spinal fluid was under pressure with a cell count of 50. The Wassermann reaction of the spinal fluid was positive, but arsenical and mercurial treatment did not help. After five months of illness, the patient died, and at the autopsy the typical lesions of subacute endocarditis were found, with a small hemorrhage on the external aspect of the left frontal lobe. The authors were at a loss to explain the meningeal symptoms. They referred to a similar case reported by Claude, in which there were 50 cells in the spinal fluid and in which at autopsy, softening at the base of the brain was found.

In his book, "Facts on the Heart," Cabot[3] referred to the case of a man, aged 21, who at the age of 12 had rheumatism, with a subsequent mitral lesion, and who at 21 had an acute illness with fever, and suddenly developed a left hemiplegia with stupor. The neck was possibly slightly stiff; there were positive Kernig and Babinski signs. Lumbar puncture gave a pearly fluid showing 860 cells, 70 per cent of which were polymorphonuclear and 30 per cent lymphocytes; no organisms were found. There was bilateral spasticity in the lower limbs, with a spastic, flexed left arm and slight spasticity of the right arm, with some voluntary motion. The clinical diagnosis was chronic endocarditis, acute endocarditis, hypertrophy and dilatation of the heart, cerebral embolism and abscess and acute meningitis. The patient died on the day after admission, and autopsy showed edema of the pia but no definite meningitis. The left middle cerebral artery was solidly plugged,

* Submitted for publication, July 18, 1928.

* Read at a Meeting of the College of Physicians of Philadelphia, Jan. 4, 1928.

1. Osler, William: Chronic Infectious Endocarditis, Quart. J. Med. **2**:219 (Jan.) 1909.

2. Lereboullet, P., and Mouzon, J.: Forme meningitiques de l'endocardite maligne à évolution lente, Bull. et mém. Soc. méd. d. hôp. de Paris **4**:894 (June 25) 1920.

3. Cabot, R. C.: Acute and Subacute Endocarditis, Facts on the Heart, Philadelphia, W. B. Saunders Company, 1926, p. 617.

and the anterior half of the brain, especially on the right side, showed marked softening and disintegration. Definite meningitis was not present, although it was probable that the embolus was infected. The pathologist was unable to explain the pus in the spinal fluid but thought it might have come from the disintegrated tissue of the brain. The heart showed chronic and acute endocarditis.

Smith and Brumfiel [4] reported the case of a white man, aged 36, with a subacute endocarditis involving the aortic valve. In the hospital, the patient developed photophobia, stiff neck, severe occipital headache, a positive Brudzinski sign and an equivocal Kernig sign. Lumbar puncture showed an opaque fluid with a cell count of 2,400, with 90 per cent polymorphonuclear cells. In spite of the fact that it was not possible to demonstrate meningococci, several doses of antimeningococci serum were administered, and within ten days the fluid became clear, with a cell count of 45. Blood cultures demonstrated *Streptococcus viridans*. The patient improved and left the hospital, but suffered afterward from hemiplegia, gradually failed, and died after an illness of approximately ten months.

Libman [5] spoke of meningismus as "A much neglected but valuable symptom of subacute bacterial endocarditis, of all degrees of severity, in the infectious period."

In his work, "Diseases of the Heart," Vaquez [6] spoke of a meningeal form of acute endocarditis, and said that it is distinguished by a predominance of cerebral symptoms, headache, pain in the spine, stiffness in the neck and vomiting.

Fiessinger and Janet [7] spoke of a patient with endocarditis who was under observation for six weeks. He had a double aortic lesion, headache, photophobia, no rigidity of the muscles of the neck and a slight Kernig sign. A lumbar puncture showed a clear spinal fluid, with 32 cells. Blood culture was positive. Autopsy showed a lesion at the aortic valve and a congestive type of meningitis.

PERSONAL CASES

During the summer of 1926, I saw a woman, aged 45, who had a loud mitral murmur which had been present since childhood. She had been treated for pyelitis, had improved, and when I saw her was afebrile. She complained of weakness and malaise. She suddenly developed severe headache, vomited, and on examination showed a stiff neck, photophobia and positive Kernig and Babinski signs. She did not lose consciousness, but was quiet and desired to be left alone. After several days these symptoms passed, to recur in ten days with a transient paralysis of the left arm and with the left pupil larger and more sluggish than the right. She was unconscious for three hours and afterward was drowsy and quiet. She improved in a short time and left the hospital, but died suddenly a few days later. Her condition was not well studied, as she was under the care of three different physicians in a short time.

Shortly afterward, during the winter of 1926-1927, I attended a girl, aged 17, who had a loud mitral murmur dating back to childhood, the result of rheumatism.

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4. Smith, F. Janney, and Brumfiel, Daniel M.: Meningitis Complicating Subacute Bacterial Endocarditis with Report of Case, Am. Heart J. **2**:446 (April) 1927.

5. Libman, Emmanuel: A Consideration of the Prognosis in Subacute Bacterial Endocarditis, Am. Heart J. **1**:25 (Oct.) 1925.

6. Vaquez-Laidlaw: Acute Endocarditis, Diseases of the Heart, Philadelphia, W. B. Saunders Company, 1924, p. 251.

7. Fiessinger and Janet: La forme "raccourcie" de l'endocardite maligne du type Jaccoud-Osler, Bull. et mém. Soc. méd. d. hôp. de Paris **4**:1443 (Nov. 26) 1920.

She had slight fever for a week and then had an embolus with a right hemiplegia and aphasia. She lived for five months, regained her speech and some use of her arm, but died of exhaustion. She had a constantly elevated temperature for the entire period of the illness.

Within a month after I first saw this patient, I saw two other girls with a similar history, who developed high fever; both had emboli in the brain with right hemiplegia. Both these patients had innumerable petechiae on the arms and legs, and both died before their conditions could be properly studied. I mention these patients only to indicate that, with this experience, I may be a little biased in the diagnosis of the case I am about to report.

A white boy, aged 18, had had chorea and rheumatism at 7, which were followed by endocarditis. He was the third and youngest child of healthy parents and and his two brothers were well. He had not had other illnesses. The tonsils were removed after the attack of rheumatism. On March 25, 1927, he had a slight pain over the appendix but did nothing about it. Three days later, he came to my office complaining of slight pain and tenderness over the appendix. The temperature was 99.4 F., the pulse rate 70, the leukocyte count, 14,000. The next day he was better, but on the third day the temperature was 100.6, the leukocyte count 10,700 and a surgical consultant thought that he was developing some acute infection and that, while he might have a mild form of appendicitis, this was not the cause of the symptoms.

Physical examination at this time did not show any abnormality except a mitral systolic murmur of moderate intensity and an enlarged thyroid. The same day, March 30, while on the bed-pan, he felt a sudden numbness in the left arm and leg, and shortly afterward was unable to swallow capsules and could swallow food only with difficulty. These symptoms persisted and the difficulty became worse; by April 2, he could not swallow at all, and speech was slurring and thick, so that one had to pay strict attention to understand him. There was no loss of consciousness, but severe headache, photophobia, stiff neck, pain in the back, and a Kernig sign were present; the knee jerks were absent. The faucial muscles on the right side were paralyzed; there was some weakness of the muscles of the right side of the face and moderate weakness of the right arm and leg. The temperature was 100; pulse rate, 68, and respiratory rate, 18. Lumbar puncture revealed 614 cells, 50 per cent lymphocytes, 16 polymorphonuclear and 34 per cent ependymal cells. Smear and culture gave negative results. Inoculation into guinea-pigs with the spinal fluid gave negative results. The Wassermann reactions of the blood and spinal fluid were negative.

In spite of the fact that the smear and culture gave negative results, it was thought best to administer antimeningococcic serum. This was done both intraspinally and intravenously until more than 100 cc. had been given in the course of a few days. Pus continued to be present in the spinal fluid, but organisms were not found. The symptoms gradually improved, and by April 12, he was able to swallow, and feeding by gavage, which had been instituted, was abandoned. Paralysis of the faucial muscles was still present, and there was weakness in the right arm and leg. Speech was better, and stiffness in the neck and the Kernig sign had disappeared. The heart murmur remained the same. Blood counts made during this period showed hemoglobin, 87 to 81 per cent; red cells, from 4,600,000 to 4,210,000; white cells, from 17,000 to 10,700. A differential count revealed: polymorphonuclears, 79 per cent; lymphocytes, 12; large mononuclears, 3; transitionals, 2; eosinophils, 3 and basophils 1 per cent. Urinalysis revealed: specific gravity, 1.016; amber, flocculent urine; a faint trace of albumin; no sugar; many hyaline and granular casts; many cylindroids; white blood corpuscles, two or three to each high power field; occasional epithelial cells; urates, and mucus threads.

On April 25, another lumbar puncture showed fluid, not under pressure, with a cell count of 43; lymphocytes, 92 per cent; polymorphonuclears, 4 per cent; endothelial cells, 4 per cent. Two blood cultures remained sterile. The patient refused permission for additional cultures.

From April 25, 1927, until Sept. 19, 1927, when he died, the patient had a continuously elevated temperature, at times as high as 103 F., but usually not higher than 101. From time to time he developed numerous petechiae over the trunk, and Osler's nodes on the hands. He also developed reddened, painful swellings in the forearm and leg, apparently of embolic origin, which would last for a few days and then disappear. The embolic phenomena were associated with heightened temperature, usually up to 103 F. The paresis in the right arm and leg disappeared entirely; he could talk naturally and swallow perfectly. Cardiac symptoms or decompensation were never present. He complained of a great deal of pain in the lumbar region, at the site of the lumbar puncture. The spleen was never frankly palpable. He showed no sign of emboli in the spleen or kidney. At times the murmur seemed louder than at others.

Despite the fact that there was a negative blood culture, no enlargement of the spleen, and no cardiac phenomena other than the murmur, I believe that I was justified in making a diagnosis of subacute endocarditis with cerebral embolism. The patient's history of rheumatism and chorea, the cardiac murmur, the prolonged fever and the embolic phenomena convince me that this diagnosis is correct. In Osler's masterly presentation of this subject, he emphasized the fact that with a history of rheumatism, a cardiac murmur, a prolonged fever and embolic phenomena, such as petechiae and the nodes that bear his name, the diagnosis is almost certainly subacute endocarditis. A positive blood culture, of course, confirms the diagnosis, but Osler secured positive cultures in only three of the ten cases reported. Malaria was looked for and excluded because of failure to find the organism. There were never any symptoms to make one think of tuberculosis.

At the beginning of this illness two other diagnoses were offered: The first one meningitis, which seemed almost surely correct, because of the headache, photophobia, stiff neck, positive Kernig sign, irregular paralyses, and 600 cells in the spinal fluid; however, not any organism was found in smears or cultures or by inoculation, and after a lapse of two weeks the symptoms ameliorated decidedly. If it had been any other form of meningitis than that due to the meningococcus, the patient would almost surely have died. If it had been the latter, one almost surely would have found the organism. The second diagnosis was epidemic encephalitis. This protean disease is at times difficult to recognize, being often diagnosed when the symptoms and signs are bizarre, but a triad of symptoms usually characterizes this disease: fever, somnolence and ophthalmoplegia, whatever other symptoms may be present. Of these there was only one present — fever. It is true that a slight droop of the right eyelid was noticed, but somnolence and double vision, which I believe are almost "sine qua non" for the diagnosis of this disease, were not present. I shall not attempt to discuss this phase of the matter further, but shall leave it to my colleague, Dr. Weisenburg.

COMMENT

One other possibility has not been mentioned, namely, aneurysm of a cerebral artery. French writers speak of "arterial ectasias" which may occur in endocarditis as a result of the projection of debris from the heart valve against the vessel wall. They may involve any of the peripheral arteries. They form rapidly

and may persist without change or recede slightly, according to Vaquez.[8] Friedman[9] spoke of aneurysms of the cerebral arteries as a result of embolism of the vessel wall. They are small and are not due to syphilis. Rupture or oozing may take place. In oozing, according to this author, signs of meningeal irritation may appear, such as stiff neck and a positive Kernig sign. Usually, the cell count is increased and the spinal fluid is slightly bloody or yellowish, due to derivatives of the blood pigment. He said that aneurysm of the basilar artery exerts pressure chiefly against the pons, medulla or peduncle. With such a lesion the patient usually experiences pain in the occipital region and difficulty in moving the head. Compression of the pons may be evidence with symptoms of alternating subacute hemiplegia or bulbar paralysis. Manifestation of irritation or paralysis are sometimes referable to the individual cranial nerves (from the fifth to the twelfth). In aneurysm of the basilar artery, hemiplegia shifts from one side to the other without ever disappearing completely, until finally the condition becomes diplegia or paraplegia. I do not believe, however, that I was dealing here with an aneurysm of a cerebral vessel, although it is certainly a possibility. It is likely that the lesion, whether it was an embolus or arterial ectasia, was in the basilar artery or one of the branches. The numbness on the left side, followed by the paresis on the right, the difficulty in speech and deglutition, all point to a lesion in this neighborhood. Just how the symptoms of meningitis were produced is not clear, unless there was oozing from an aneurysm. There is no doubt in my mind that this patient suffered from subacute endocarditis. The subsequent course of the disease, the prolonged fever, the petechiae, the Osler's nodes and the other embolic phenomena, with almost complete disappearance of the neurologic phenomena, force me to believe that the disorder was primarily cardiac and not meningeal or cerebral.

DISCUSSION

DR. T. H. WEISENBURG: When I first saw Dr. Ullom's patient I made a diagnosis of meningitis because of the presence of headache, rigid neck, pain in the back, Kernig's sign and the serologic manifestation of an increase of the cell count. In addition, he was somewhat stuporous and had the symptoms of definite right hemiplegia with paralysis of the right palate, some nystagmus and a suggestion of weakness of the right external rectus. The meningitic symptoms cleared up rapidly, and there remained the picture of a bilateral cerebral involvement in that he showed from the onset a numbness in the left limbs, which persisted for some time, right hemiplegia with the attending increase of reflexes and the Babinski phenomenon, weakness of the right palate, with an accompanying difficulty in talking and swallowing, and later, a drooping of the right upper lid. These symptoms obviously indicated multiple lesions in different parts of the cerebrum and brain stem. A diagnosis of encephalitis seemed therefore most probable, although it was recognized that meningitic symptoms are only rarely present in the beginning of encephalitis, and that persisting fever was equally uncommon, although I have recorded a case of encephalitis in which the temperature ranged from 99 to 102 F. for a period of five or six months.

During my connection with this patient, which was about a month, I held to the diagnosis of encephalitis. During this period, Dr. Ullom constantly argued that he had seen other patients with this clinical picture and with an accompanying cardiac condition, and held to the diagnosis of a subacute endocarditis with com-

8. Vaquez-Laidlaw: The Prolonged Form of Malignant Endocarditis, Diseases of the Heart, Philadelphia, W. B. Saunders Company, 1924, p. 256.

9. Friedman, E. D.: Intracranial Aneurysms, Cecil's Medicine, Philadelphia, W. B. Saunders Company, 1927, p. 1310.

plicating meningeal and cerebral symptoms. The further course of the case, especially the development of numerous petechiae over the trunk and of painful swellings in the forearms, fingers and legs, apparently of embolic origin, proved Dr. Ullom's contention without any doubt.

I have since looked up the material in the Neuropathological Laboratory of the Philadelphia General Hospital and have found a record of an almost similar case. A man, aged 29, gave a history of rheumatism complicated with nephritis and endocarditis. Shortly before death he developed all the symptoms of what was thought to be an acute meningitis. There were, on the other hand, no cerebral symptoms such as were present in Dr. Ullom's case. The spinal fluid showed 6 cells, a trace of globulin, no organisms, a negative Wassermann reaction and a gold curve of 4444431000. Pathologically, there was marked swelling of the lining cells of the intima of the smallest blood vessels of the brain. So great was the swelling in certain places that vessel occlusion had occurred with degeneration of small areas of the cortex. A reactive meningitis in the form of a serous meningitis was the explanation for the clinical meningeal condition.

What is the pathologic explanation in Dr. Ullom's case, and how can the symptoms be accounted for? It must be remembered that the patient first showed the symptoms of meningitis, then multiple involvement in different parts of the brain and brain stem, and that the meningitic and neurologic symptoms disappeared before the onset of the symptoms resulting from multiple emboli.

The meningitic symptoms can be explained on the theory of a serous reactive meningitis. This is not at all uncommon in acute infections. It is more difficult to explain the cerebral pathologic changes. The fact that these symptoms disappeared obviously points to a toxemic basis. If one can reason from the evidence furnished by the pathologic case quoted, it would seem that the swelling of the lining cells of the intima was of only a temporary character, this accounting for the disappearance of the symptoms, and that the emboli resulting from endocarditis came later.

The lesson to be learned from this case is that if a patient has a rheumatic history and endocarditis, if meningitic symptoms of a mild character subsequently develop without the presence of an organism in the cerebrospinal fluid, with cerebral symptoms indicating diffuse pathologic change either of a temporary or of a permanent character and with an accompanying persistent fever of a mild grade, suspicion should be directed to the endocardial condition as the underlying cause.

ANTERIOR POLIOMYELITIS AND SUPERINFECTION WITH EPIDEMIC ENCEPHALITIS

Report of a Case *

MILTON C. BORMAN, M.D., MONTGOMERY, W. VA.

Occasional superinfections in diseases of the central nervous system have been reported. Höglund[1] recorded the superinfection with relapsing fever in chronic epidemic encephalitis. Excellent results have been reported by numerous writers

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* From the Montgomery Clinic.

* Submitted for publication, June 4, 1928.

1. Höglund, G.: Finska läk.-sällsk. handl. **69**:402, 1927.

in the treatment of patients with general paresis by superinfection with malaria. The finding of anterior poliomyelitis and superinfection with epidemic encephalitis in a patient with probably defective germ plasm seemed to be of sufficient interest to be recorded.

REPORT OF CASE

A white girl, aged 2 years, suddenly became ill, the onset being characterized by irritability and elevated temperature, followed twenty-four hours later by paralysis of the right leg. The paralysis was complete, and she has never recovered. The right leg atrophied subsequently, and there was inability to extend the leg on the knee. The child had always walked without braces or support. Except for lameness, she appeared to be a normal healthy child.

At the age of 10 years, during the influenza epidemic in 1918, the patient again became ill. Her physician stated that at that time there was some disturbance of vision, and she was somnolent and stupid for about two weeks. Two other patients in the immediate vicinity were stricken with a similar illness. The diagnosis made in each of the three cases was epidemic encephalitis. The patient recovered from this illness, but it was noted that she gradually lost interest in her studies and other activities. She became fatigued quickly, seemed unable to concentrate attention and showed lack of purpose and increasing vacillation. At the age of 13, an "inward nervousness" was felt in the right upper extremity, which later developed into a tremor; at the time of examination, when the patient was 20 years old, this was her major complaint. Excitement and emotion increased the tremor, which was not intentional and disappeared at night. Prior to the time she had encephalitis, the patient had had occasional attacks of somnambulism, but there had been none since that time. A maternal aunt and two maternal great aunts were extremely unstable. A brother, aged 21, was being treated in an institution for grand mal epilepsy.

Mentally, the patient appeared bright and cheerful, answered questions intelligently and readily, was embarrassed, excessively modest and easily confused. There was no evidence of a psychosis. She did not place any particular emphasis on her paralysis, but was worried considerably about the tremor because it was embarrassing to her socially.

Physical examination revealed atrophy of the right foot and leg with inability to dorsiflex the ankle on the foot or to extend the leg completely on the knee. The right knee and ankle reflexes were absent. There was a mild gross tremor of the upper extremities, greater on the right than on the left. Hypertonicity of the muscles of the upper extremities was noted. Slight tremor of the lips and tip of the tongue and a flattening out of the facies were seen. Laboratory studies revealed a negative Wassermann reaction.

The clinical diagnosis was flaccid paralysis with atrophy of the right lower extremity subsequent to anterior poliomyelitis; parkinsonian syndrome following superinfection with epidemic encephalitis.

News and Comment

MEETING OF AMERICAN NEUROLOGICAL ASSOCIATION

The Fifty-Fifth Annual Meeting of the American Neurological Association will be held in Atlantic City, June 3, 4 and 5, 1929.

INTERNATIONAL NEUROLOGICAL CONGRESS

This meeting, which was initiated by the American Neurological Association, will be held in Berne, Switzerland, from Aug. 31 to Sept. 6, 1931, inclusive. So far, favorable responses have been received from the following countries: Austria, Belgium, Canada, Denmark, France, Germany, Great Britain, Holland, Hungary, Italy, Poland, Rumania and Switzerland. All of these countries have appointed delegates, and a smaller organization committee made up from these delegates will meet in Berne on Aug. 29 and 30, 1929, to effect a permanent organization and to determine on the program and other matters relating to the congress. In order to facilitate the work of the organization, Dr. Charles Dubois, 20 Falkenhöheweg, Berne, Switzerland, has been appointed corresponding secretary in Europe. Dr. Henry A. Riley, 870 Madison Ave., New York, is the American secretary, and Dr. Bernard Sachs is chairman of the American committee.

THIRD INTENSIVE POSTGRADUATE COURSE OF NEUROLOGY AND PSYCHIATRY IN VIENNA

The third intensive postgraduate course of neurology and psychiatry will be given in English under the auspices of the American Medical Association of Vienna between May 21 and June 29, 1929. Applications should be forwarded to Dr. E. Spiegel, Vienna I, Falkestrasse 3.

Abstracts from Current Literature

THE STRUCTURE AND ACTIVITY OF THE HORTEGA CELLS IN PATHOLOGIC PROCESSES. H. G. CREUTZFELDT AND A. METZ, Ztschr. f. d. ges. Neurol. u. Psychiat. **106**:18 (Dec.) 1926.

In 1924, Metz and Spatz reported their investigations on the supporting network of the nervous system as stained by del Rio-Hortega's silver carbonate method. The microglia cells were called by them Hortega cells. The present article is a study of the activity of the Hortega cells in pathologic processes.

Nissl first described the rod cells as a special glial element, and so opened the way to the discovery of the Hortega cells. Alzheimer described them in his work on general paralysis and showed their manifold forms. Since then only a few studies of these cells have been made in Germany. Of the Spanish investigators, Achucarro studied these cells intensively. He showed, by his own stain, that the rod cells are strongly branched, that the majority are multiradiated and that in the earliest period after an injury they take on a phagocytic function and take up fat. After Cajal's gold sublimate stain established the astrocytes as a special form of glia, it was evident that these cells did not belong to this class. Later, Hortega showed that they were a subform of his microglia. He showed that under pathologic conditions the microglia take on phagocytic activity. These cells can engulf red and white corpuscles and connective tis ue debris. From experiments Hortega concluded that of all the supporting cells of the nervous system the microglia alone can form gitter cells, and that they are responsible for the occurrence of these in cerebral softenings.

Creutzfeldt and Metz report the changes in the Hortega cells in various pathologic states as follows:

1. *Chronic Degenerative Processes.*—Under this heading are included senile dementia, senile atrophy of the brain, dementia praecox, Huntington's chorea, Alzheimer's disease, epilepsy, and cases of arteriosclerotic dementia with manifestations not related to the vessels. In all these conditions, the Hortega cells showed definite changes. Their number either showed no increase or was very slightly increased. They occurred singly and only rarely in pairs. The nuclei were often small and oval, sometimes large. They often showed little protuberances. Some were pale. The protoplasm was increased in amount, the processes being wider and the perinuclear protoplasm increased in amount. The cell branching was about normal except that in some cells it was more pronounced, many small processes branching off from the protoplasm.

2. *Acute Degenerative Processes.*—In a few cases of imbecility and dementia praecox in which the patient died after periods of excitement or in coma, the Hortega cells showed marked changes. In some instances they were not increased and had fine threadlike processes. In such cases the perinuclear protoplasm was increased. In other places the Hortega cells were much increased and mitoses were seen. These cells were round and large. Many cells had short, stumpy processes which were broadened out, but the increase in protoplasm was seen most clearly in the perinuclear protoplasm. Often, cells were seen destroying nerve cells; sometimes two or three cells were so closely united as to make them one.

3. *Meningo-Encephalitis.*—Purulent and tuberculous meningitis were studied. The number of Hortega cells in the cortex was increased They were less broadened out; bipolar forms were frequent. The processes were broad and the nuclei often rounded. The perinuclear protoplasm was often increased and contained vacuoles. Ganglion cells practically always had one, sometimes two, satellite Hortega cells.

4. *General Paralysis.*—In this disease there is a marked increase in the Hortega cells; their processes are broadened, much branched and long, while the perinuclear

cytoplasm is not particularly increased. While the picture of the Hortega cells is typical, numerous exceptions occur. The forms of the Hortega cells depend on the layer of the cortex involved. In the third cortical layer, many rod cells occur, while in the upper and lower layers, different forms occur. In Ammon's horn, every layer contains a different form of Hortega cells when the latter are perceptibly increased. The Hortega cells show varied relations to the ganglion cells. Frequently they partially surround the latter with fine, threadlike processes. Often also, they completely surround the ganglion cells, and later two or more Hortega cells can be seen entirely surrounding a ganglion cell. The Hortega cells are found in greatest numbers in the vicinity of two processes—inflammatory and degenerative. They are much increased in areas of inflammation in general paralysis, and also in areas where there is apparent degeneration of cells.

5. *Special Focal Reactions.*—The brain of a general paralytic patient who had had many convulsions and who died in status epilepticus showed a large number of focal formations—glial stars, rosets and nodules. These were not in relation to ganglion cells; they were found in the medulla of the central cortex, the gyrus hippocampi and Ammon's horn. Glial stars were frequent and consisted of a few Hortega cells; they showed transitory stages to rosets containing many Hortega cells.

6. *Circulatory Disturbances.*—The changes in the Hortega cells as a result of circulatory disturbances are different from those described elsewhere. The Hortega cells in an area of softening are much increased, while outside this area they are not much increased. The deeper one goes in the cortex, the more numerous and the larger these cells become. They show all types of transition to gitter cells, and in fat preparations they appear as gitter cells with characteristic structure. They become more and more round and their processes shorter and more stumpy as they change to gitter cells. All of the circulatory disturbances in many other cases showed similar characteristics.

7. *Senile Plaques.*—Since the work of Alzheimer, it has been known that the senile plaques are formed of glia cells. The glia cells which are found in and around these plaques are Hortega cells; they are unipolar or bipolar in type. The cells of unipolar type penetrate into the center of the plaque where the nucleus lies. Hortega cells are active in the destruction of the plaques as well as in their formation.

As Hortega has pointed out, these cells play an important rôle in the central nervous system. They take up pathologic and formed products and consume them. They alone of the glial elements can form gitter cells. Creutzfeldt and Metz found in the course of their investigations that Hortega cells never multiply alone; that their hypertrophy and hyperplasia occur only as the result of diseases of other elements, especially of the nervous connective elements. Their observations, too, showed that in the different processes in which they are concerned the Hortega cells take up and consume pathologic waste products, while they grow and increase and change to gitter cells. They could attribute no further activity to them; these investigators think also that they may serve to fill up space in areas of destruction.

Mitosis may often be seen among the Hortega cells, although in places where there is marked increase in them, mitoses often do not occur. Hortega believes that amitotic multiplication probably occurs in these places. The daughter cells may remain attached to the mother cell by their protoplasm, but eventually they become separated. The multiplying power of the Hortega cells is great and proliferation may be rapid. As Hortega showed experimentally, they may be present in great numbers on the edge of a focus twenty-four hours after injury occurs.

The increase in the Hortega cells is accompanied by a great increase in the number of forms. These cells are extraordinarily polymorphous; there are unipolar, bipolar, multiradiated, and round Hortega cells. Achucarro explains the polymorphism by the fact that their shape is an adaptation to the structure of the surroundings. Hortega asserts that the protoplasm of these cells is extraordinarily plastic; their form is determined by the space between the nervous sup-

porting structure. They bore into the spaces between the nerve structures, parallel to the cells and fibers, and they surround these structures.

ALPERS, Philadelphia.

THE PATHOLOGY OF AMYOTROPHIC LATERAL SCLEROSIS. Jo NAKAMURA, Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **29**:141, 1927.

Histologic examination of the central nervous system in four cases of amyotrophic lateral sclerosis showed that the lesions were essentially inflammatory in nature; curiously enough they were also precisely in the same localization as in poliomyelitis, i. e., in that part of the cord which is supplied by the anterior spinal artery. Although the process was less marked than in genuine poliomyelitis, there was no doubt as to its inflammatory character. The characteristic localization of the process—in the region of the anterior horn cells—precluded the possibility of the hyperemia being due to pneumonia, from which the patients had died. It must therefore be assumed that the inflammatory process, which was also found in the cerebral cortex in two cases, as Naitto had previously shown, is the specific and characteristic type of lesion in amyotrophic lateral sclerosis. A study of the exudate did not shed much light on the character of the inflammatory process other than an increase of adventitial cells and of lymphoid cells. The inflammatory process in the cerebral cortex was identical with that in the anterior horn cells of the cord. It was noteworthy that the largest cells, the motor cells of the anterior horns of the cord and the large pyramidal cells of the cerebral cortex, were the first to be affected by the inflammatory process.

The usual lipodystrophic degeneration of the ganglion cells, said to be characteristic of amyotrophic lateral sclerosis, were found in these cases. The posterior horn cells showed no lipoidosis. In the cerebrum the lipoidosis was limited to the large ganglion cells. The dystrophic disturbance presented changes analogous to those in the senium (a rich deposition of pigment), in spite of the fact that the patients were only in the fourth and fifth decades of life. The sections also showed other changes in the ganglion cells, but it was impossible to determine whether these were not complications of the essential pathologic process. The Bielschowsky stain revealed that in areas in which the cells were unusually shrunken the fibrils were all broken up and the dendrons fragmented. In the cases in which the lipoidosis was not as yet far advanced, the cells were filled with a finely pigmented network.

The cellular degeneration in the anterior horns showed a definite order of invasion; the cells first affected were the most peripherally situated ventral and dorsomedial cells; next were the inner cells, and finally those lying in the ventrolateral region. This may have been a coincidence, but it was striking.

The pyramidal tracts were degenerated in the anterior as well as in the lateral columns; the perivascular accumulation of fatty granular cells was abundant evidence of destruction of myelin. None of the cases showed degeneration of the posterior column, but some of them showed definite involvement of the anterolateral columns. There was marked degeneration of the anterior nerve roots which corresponded well with the degree of degeneration of the ganglion cells.

There was nothing unusual about the glial process; it merely represented a compensatory replacement of the degenerated parenchyma. This was especially noticeable in the Betz cells although it was found also in the anterior horns in which there was a definite increase of glial granules; in this localization, however, the process led to shrinkage rather than to replacement of the degenerative process. On the whole, the glia showed little special activity.

Although the patients were not aged, the blood vessels showed moderately advanced sclerosis. In all cases there were evidences of meningofibrosis and of a definite inflammatory process in the longitudinal sulcus. The pial changes in the brain were similar to those in the cord.

SUMMARY

In amyotrophic lateral sclerosis, there is an inflammatory process, the localization and character of which are identical with those observed in poliomyelitis; they are, however, more acute in the latter. The inflammatory process is followed by a severe trophic disturbance of the largest ganglion cells in the cord, medulla oblongata and cerebrum. In all these localizations the cellular process is one of lipodystrophy of presenile character. Whether the peculiar vascular supply of these structures or an extension of the process to a definite vascular region is the cause of the peculiar localization, or whether in this disease there is a peculiar form of tropism cannot be determined.

KESCHNER, New York.

CEREBELLAR CHANGES IN EPIDEMIC ENCEPHALITIS. AKIRA KAWATA, Arb. aus dem Neurolog. Inst. an der Wiener Univ. **29**:226, 1927.

Kawata examined a series of cerebellums from cases of chronic encephalitis to determine if the dystonic-dyskinetic symptoms of chronic encephalitis are a result merely of striopallidal pathology or if other parts of the brain, especially the cerebellum, are involved. Hohman had found changes in the nucleus dentatus in cases of encephalitic parkinsonism. The granule cells were but slightly involved while the Purkinje cells showed definite dendritic changes similar to those seen in amaurotic idiocy. Hyperchromatosis of the nuclear wall in the Purkinje cells and infiltration of the meninges have also been described. Still earlier, O. König found the Purkinje cells reduced to one-third, the granule cells diminished and intense degeneration in the nucleus dentatus. Other authors pointed out that the cerebellar cortex remained free from changes. Stern and Kreuzfield emphasized the fact that inflammatory changes were limited to small areas while the degenerative changes were more diffuse. They inferred that the latter changes were due primarily to a toxin. Cetverikov holds that the pathologic changes in parkinsonism involve only those parts of the brain exposed to the influence of the cerebrospinal fluid. Among these is the cerebellum.

Kawata examined the vermis superior, lobus anterior, lobulus simplex, lobulus semilunaris superior, lobulus semilunaris inferior, lobulus biventer, tonsil, flocculus and the nucleus dentatus in cerebellums from eight cases of chronic encephalitis with parkinsonism. He concluded that the cerebellar meninges are as a rule little affected. Minimal thickenings and isolated cellular infiltrations indicate a secondary irritative process rather than primary involvement. In the cerebellum itself the changes in the cortex are apparent. It is surprising that these have been overlooked by most authors with the exception of Hohman and König. There is a decrease in granule cells which varies in intensity. The process is discontinuous, affecting both the deep and superficial parts, but is pronounced in the flocculus. This is explained by Cetverikov by the fact that this part comes in most intimate contact with the cerebrospinal fluid.

The changes in the Purkinje cells are of greatest interest. They are similar to the changes seen in senility and occur irrespective of the age of the patient. Among them are included swelling and tortuosity of the dendrites, degeneration of the cells and hyperchromatosis of the nuclear walls. Finally, there is a decrease in the number of cells. The observations in the cortex are typical and occurred in all cases although to a varying degree. In every case was profound alteration in the nucleus dentatus. In addition to the disappearance of cells, all of the cellular changes known to pathology, including swelling, shrinking, vacuolization, hyperchromia, hyperchromia of the nuclear wall, and homogeneous nuclear shrinkage were present. A most striking process was seen in the molecular layer. It consisted of small areas of tissue necrosis with vacuoles into which projected processes resembling swollen axis cylinders or swollen glial processes. The similarity of the disintegration of the tissue to the changes seen in senility emphasizes the severity of the process. Since similar changes

have also been described in general paralysis, Kawata regards them as the reaction of the organism to any kind of damage, irrespective of its nature, rather than as a specific reaction to any certain toxin.

When the clinical symptoms are interpreted in terms of the pathologic changes present, it is seen that in all eight cases the outstanding clinical picture was the akinetic-hypertonic syndrome. In only one case was there any ataxia and in one other a positive Romberg sign. In spite of the considerable cerebellar damage present, there were practically no so-called cerebellar symptoms. The tremor may be regarded as an exception to this, and it is not impossible that this symptom is conditioned by the extensive involvement of the nucleus dentatus in all cases. The relative absence of cerebellar symptoms leads Kawata to the assumption that there must have been a rapid compensation for the gradual loss of cerebellar function through slow involvement.

KAMMAN, St. Paul.

OBSERVATIONS AND RESULTS FROM INTRACRANIAL SECTION OF THE GLOSSOPHARYNGEUS AND VAGUS NERVES IN MAN. TEMPLE FAY, J. Neurol. & Psychopath. **8**:110 (Oct.) 1927.

The exact function of the glossopharyngeus and vagus nerves in man, especially as to their sensory values, has not as yet been definitely established. Owing to connections which exist between these nerves in the jugular foramen and peripherally, it has been impossible to judge of their specific functions following extracranial section of one or the other. Two cases were encountered in which intracranial sections permitted certain definite conclusions. The patient in the first case, one of carcinoma at the base of the tongue on the left, had severe pain in the left ear, behind the ear, and extending to the vertex and in the throat, lower jaw and tongue. Cervical rhizotomy of the second and third posterior cervical roots on the left and intracranial section of the left glossopharyngeus nerve brought relief from all pain except that confined to the throat and ear. Later, section of the root of the trigeminus on the left did not bring about any change in the pain in the throat and in the ear. In addition to the trigeminus and the second and third cervical roots, the ramus auricularis nervi vagi completes the nerve supply of the auricle. The area supplied by the latter in the cavum conchae and cymba showed retained sensation. The "gag" reflex remained intact. Swallowing was unchanged. Pain sense remained in the pharyngeal wall and in the posterior margin of the soft palate. Taste was abolished on the posterior and anterolateral portions of the tongue. Increased salivation occurred on the left. It is concluded that the only demonstrable function of the glossopharyngeus nerve has to do with taste reception and salivary secretion. Whatever sensory fibers appear in the extracranial or peripheral course must be added chiefly from the vagus. The second case was also that of carcinoma of the tongue on the left. The patient had severe pain in the ear and throat, with some pain in the tongue and lower jaw. Subtotal (the lower two divisional fibers) avulsion of the posterior root of the left trigeminus nerve relieved pain in the tongue and lower jaw but left the pain in the ear and throat unchanged. Later, intracranial section of the roots of the left vagus completely relieved the patient of all pain in the ear and throat. In addition to the existing anesthesia in the second and third trigeminal areas, including the tragus and anterior wall of the internal auditory canal, this second operation produced anesthesia of the posterior wall, the concha, the anthelix and the antitragus. There was also a small area behind the ear, over the base of the scaphoid and in the region of the auricular mastoid fossa in which all cutaneous sensation was lost. The soft palate was paralyzed; there was great difficulty in swallowing, and the left vocal cord was paralyzed. The "gag" reflex was absent on the left. Taste was present. The pharynx on the left was anesthetic. It is concluded that the vagus supplies common sensation to the pharynx and larynx, dispersing these fibers directly by its own branches and indirectly by filaments carried by the extracranial trunk of the ninth nerve—and common sensation to a portion of the external ear. This nerve is the chief

motor supply of the pharynx and larynx and probably the soft palate. It is responsible for the "gag" reflex and for reflex pain in the ear due to involvement of its pharyngeal branches. The motor fibers to the vocal cord leave by the vagus root and not by the vagus accessory, as has been claimed. In analyzing the previous work of Doyle and of Adson on so-called glossopharyngeal neuralgia, the author concludes that relief of the pain points to the fact that the glossopharyngeus nerve probably carries these sensory fibers in its extracranial course or that the branches and roots of the vagus, which were also sectioned, destroyed the pain arcs. The term "vagal auricularpharyngeal neuralgia" is suggested as more correct.

FAVILL, Chicago.

THE DIFFERENTIAL DIAGNOSTIC SIGNIFICANCE OF CORTICAL AND MESENCEPHALIC HYPERKINESIAS. L. J. OMOROKOW, Ztschr. f. d. ges. Neurol. u. Psychiat. **106**:79 (Dec.) 1926.

Omorokow studied in particular the types of hyperkinesia found in Koschewikoff's epilepsy and in the myoclonic form of epidemic encephalitis; twenty-eight patients with the former were operated on. Omorokow, in 1922, reported that the disease process has its origin in the cortex. The pathologic change is a circumscribed encephalitis; in two cases, however, the author found a cysticercus solitarius in the prefrontal convolution. Of the twenty-eight patients operated on, 42 per cent lost the hyperkinesias completely; consequently, it was concluded that the localization of the cause of the hyperkinesias lay in the cortex. The etiology of the hyperkinesia of epidemic encephalitis, however, is not clear.

Omorokow studied hyperkinesia by two methods—myographically and tromographically. In the first method a convulsing muscle was attached to a revolving drum by a writing point, and records were made of the hyperkinesia. Since the activity of only a single muscle can be recorded in this way, the method of Pierre Marie was used: in this method the oscillations of the entire limb as a result of a convulsion were recorded. The patient holds a Marey tambour in his hand, with a weight attached to the membrane. This tambour is connected with the drum by an elastic tube. The convulsions that shake the hand, shake the tambour also; the weight on the membrane swings back and forth, and these movements are transferred to the writing point which records on a revolving drum. By this method it was possible to record the series of events in a convulsion and to observe the increase and decrease in the convulsions with voluntary movements.

Omorokow concludes from his studies that the characteristics of mesencephalic convulsions are entirely different from those of cortical convulsions; that they are observed as the result of epidemic encephalitis and other diseases with lesions in the striopallidal system. The convulsions in Koschewnikoff's epilepsy, on the other hand, occur as the result of lesions in the motor cortex.

The convulsions of Koschewnikoff's epilepsy are characterized thus: 1. They are of the jacksonian type, and occur often at night. There are pyramidal symptoms, paresis and paralysis, often with cerebral atrophies and contractures. 2. They are localized in different muscles. Agonists and antagonists are simultaneously contracted and produce movement of the extremities. They are not imitable. The movements are organized, chaotic, yet stereotyped. 3. They are not uninterrupted. There are active phases and phases of rest occupying from three to four records. 4. They are not stopped by sleep or by voluntary movements. They are increased by excitement. 5. The hyperkinesia is unilateral.

Convulsions originating in the mesencephalon differ as follows: 1. There are no attacks; parkinsonian phenomena are observed; pyramidal symptoms and contractures do not occur. 2. The convulsions are strictly localized in synergistic groups with inhibition of the antagonists. As a result, regular, shaking movements occur which are easily imitated. They are similar to the automatic movements of sucking, grasping, etc. 3. The attacks continue uninterruptedly without pause, with equal intervals, and all the muscle contractions have equal wave heights,

4. They are interrupted by sleep, as well as by passive and active movements.
5. They are often bilateral in the hands, the masseters, and the lips.

ALPERS, Philadelphia.

SYMPTOMATOLOGY OF FRONTAL LOBE LESIONS. JOSEF GERSTMANN, M.D., Wien. klin. Wchnschr. **40**:1133 (Sept. 8) 1927.

The author discusses what he proposes to call frontal astasia and abasia. He divides the syndrome into four parts. (1) What has been for years considered as a frontal ataxia; but there has, however, remained considerable opposition to such a term as it seemed probable that this ataxia was due to generalized pressure or to contrecoup pressure on the cerebellum. During the war Gerstmann had occasion to see sufficient lesions of the frontal lobe to convince him that the question of cerebellar involvement could be definitely excluded. He found that lesions of the prefrontal area, especially of the basal medial portion, produced disturbances of equilibrium which lesions of the posterior part of the frontal lobe failed to show. As a basis for this frontal ataxia the lesion is assumed to be a cortical interference of the frontopontocerebellar system; this is also the opinion of Monakow, Anton and others.

(2) The station and gait of the patient. The patient appears to have lost his sense of station. He constantly searches for his center of gravity. There is a definite tendency to retropulsion. The gait is of a hesitating type. The patient takes short unsteady steps and constantly appears to be either held back or pushed about by some invisible force. While this symptom may be looked on as a component part of equilibrium it can be easily differentiated. It may precede any disturbance of coordination and does not in any way run parallel to it. This propulsion syndrome has been most frequently found in tumors and naturally suggests the possibility that the syndrome is due to pressure on the basal ganglia. Gerstmann believes from his material that the frontal lobe is the important factor and not the basal ganglia.

(3) A gait apraxia, which has also been described by Schilder. The patient, if supported and if he does not have paralysis, is still unable to walk in any direction, especially forward. The feet seemed to be glued to the floor and he is unable to execute the movements of walking, even though he may move his legs about in bed. This symptom has been usually ascribed to lesions of the corpus callosum and Gerstmann is not prepared to dispute this greatly. He thinks, however, that the apraxia can be produced by lesions in the anterior portion of the frontal lobe.

(4) Inability to stand up from either the sitting or the lying position. This feature is rare but, when present, may overshadow the other symptoms. Should the patient be aided to his feet he will be unable to stand but will sink to the floor en masse as the knees and hips give way under his weight. When lying in bed the legs may be moved about fairly freely so that one would not appreciate the difficulty to be encountered on attempting to stand erect. Vogt, Marie, Förster and others have described cases with this syndrome and the lesion has been attributed to a disturbance in the foot of the first frontal convolution.

These four disturbances, ataxia, retropulsion, apraxia and atonia, appear to Gerstmann to be a syndrome of the anterior portion of the frontal lobe. They may appear alone or in combination, and one may overshadow the others so that the component parts are missed.

MOERSCH, Rochester, Minn.

THE TREATMENT OF GENERAL PARALYSIS WITH LIPOIDS. I. G. LIWSCHITZ, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:570 (Oct.) 1926.

Treatment and actual healing in general paralysis may not be a total impossibility. Spielmeyer believes that cure and healing was not out of the question and indicates isolated cases of general paralysis (Wernicke, Schulze,

Nonne) in which the patient had been cured even though defects remained after recovery.

Liwschitz attacked the problem of general paralysis with the following questions: How is it that specific treatment is valuable in all syphilitic diseases except in general paralysis? How is it that specific treatment actually makes the course of general paralysis longer? Why does general paralysis attack physically healthy and energetic persons? What is the explanation of the fact that general paralysis never occurs with tuberculosis, schizophrenia, manic-depressive psychoses or other chronic diseases?

Kowchitz's first explanation was that the antibodies are probably decreased in general paralysis. The fact that strongly positive Wassermann reactions of the spinal fluid were general in general paralysis, and that this was so with only a small amount of fluid suggested that antibodies were not scarce. The author then came to the conclusion that there is an excess of antibodies in general paralysis leading to a decrease in the sensitivity of reaction and in the ability to react to the spirochetes, some of which have been immunized by the antibodies. The question arose how to reinvest the organism with its former sensitivity by employment of the excess antibodies. The lipoids were decided on as a means by which to attain this goal. Liwschitz explains, for example, the beneficial results with malaria and recurrent fever by the fact that both of these plasmodia are rich in lipoids. Both, in addition, affect the red blood cells and by means of hemolysis produce cholesterin, lecithin, and other lipoids in the blood. In syphilitic persons, moreover, the excess of antibodies remains fixed to the cells and the latter are poisoned thereby. These facts explain why strong, powerful persons are affected with general paralysis, and why the latter never occurs with chronic diseases, because a very powerful organism is necessary to overproduce antibodies.

Liwschitz prepared solutions of lipoids and treated twenty patients with general paralysis. At first he used tissue lipoid, but later used antirabic serum. There were no outward results with this. After the injection of lipoids he gave from 4 to 5 grains of a proprietary preparation in order to increase the lymphocytosis. After from ten to fifteen injections a definite change was noticeable in the physical condition of the patients. No more injections were necessary after ten or twelve had been given. In addition to the alleviation of the physical condition the psychic trouble also became definitely better. The lipoids used in these injections must be of central origin, whether they be antirabic serum, brain lipoid, or merely brain emulsion.

ALPERS, Philadelphia.

CONTRIBUTION TO THE SUBJECT OF EPILEPSY. J. NOTKIN, J. Nerv. & Ment. Dis. **67**:321 (April) 1928.

The author comprehensively reviews the literature of the past twenty years on the subject of epilepsy from the standpoints of pathology of the brain, allergy, endocrinology, blood chemistry, autointoxication and psychogenic factors. He compares his own observations in forty female epileptic patients. In 50 per cent of these cases there was an ancestral heredity of epilepsy, somewhat higher than the average given in the literature. The importance of maternal heredity, as emphasized by Thom and Siebold, was not observed. Twenty per cent of the cases showed the occurrence of nervous or mental disease in the forebears; in 32.5 per cent of the forty cases there was a history of direct ancestral alcoholism, the frequency being higher on the paternal side. Five of the patients gave an alcoholic history, in four of whom the alcohol appeared to be a precipitating factor. Five patients gave a history of emotional shock previous to the epilepsy.

The author's observations regarding the age of onset agreed well with those of Gowers, Starr, Kraepelin and others; 75.5 per cent of the patients had the first epileptic seizure before the age of 20.

Notkin believes that the relation between the onset of menstruation and the onset of attacks is overrated, as in only five cases did both manifestations occur in the

same year. There was no case in which a convulsive seizure occurred at every menstrual period. The highest frequency was 83 per cent in one case. In thirty-seven of the forty patients a test for sugar content of the blood was made; all showed normal results. The slightest increase during the convulsion was explained by the release of glycogen in the muscles during the contraction.

Kretschmer, MacCurdy, Clark and others noted sensitiveness, egotism, irritability and emotional poverty as personality features of epileptic patients. These personality features, the author finds, are more pronounced in patients whose seizures appear early in childhood and are an indication that the typical epileptic make-up should be considered a product of the epileptic reaction, while, fundamentally, the personality may be of various types. Epileptic deterioration depends on individual personality type, and apparently not on frequency of convulsive seizures.

In all of the patients the singing, monotonous voice was observed. There was a lack of flexibility and tone modulation. Phenobarbital seemed not to have any effect on the deterioration, but withdrawal of phenobarbital over a period of months caused the spells to increase slowly but considerably. When phenobarbital was again given, it did not decrease the convulsions until after several months.

In epilepsy, the authors conclude that little has definitely accrued from the study of blood chemistry, internal secretions and allergy, for the results of different investigators have differed widely. The multiplicity of etiologic factors in single cases must be considered. Examination of the brain in early stages of epilepsy might be helpful in excluding the secondary reaction.

HART, Greenwich, Conn.

COLOR CHANGES IN CRUSTACEANS, ESPECIALLY IN PALAEMONETES. E. B. PERKINS, J. Exper. Zool. **50**:71 (Jan. 5) 1928.

The decapod *Palaemonetes vulgaris*, Stimpson, changes its color in accordance with the color of its surroundings. It is reddish brown on a dark background and pale and transparent on a light background. The change from light to dark is effected by change in shape of chromatophores containing red and yellow pigments. The pattern of the chromatophore is fixed, successive periods of expansion following intervals of contraction always showing the same design. Accompanying the change in color when a shrimp is transferred from a black to a white background there is formed, chiefly in the vicinity of the chromatophores, a blue substance which surrounds them and later permeates the tissues like a dye. This blue coloration is transitory, disappearing within two hours. Chromatophore-like bodies which are pale yellow by reflected light and slate-gray by transmitted light are irregularly distributed in the hypodermis. They contract when the red and yellow chromatophores expand, and expand when these contract. The time of change from one extreme of color to the other is approximately two hours.

In *Palaemonetes* light does not act directly on the chromatophores, but only by mediation of the eyes. Absolute darkness and coating the eyes with an opaque mixture bring about a complete contraction of the chromatophores regardless of the background. Removal of one eye does not have any effect; removal of both eyes brings on a lasting expansion which is unaffected by light or background. Anesthetics cause an expansion which is probably due to temporary blindness. Electrical stimulation did not change the chromatophores. Nerve transection does not interfere with the color responses. Peripheral and visceral nerves, or a nerve net, are not concerned with the movements of the chromatophores. There is no histologic evidence to show that the chromatophores are innervated.

Occlusion of an artery always results in a cessation of the chromatic response in the region supplied by that artery. On release of the vessel the region takes on the color of the rest of the animal. An extract of the eye stalks of *Palaemonetes* when injected into blinded animals brings about a contraction of the hitherto refractory chromatophores. Extract of eyes from

white-adapted shrimps induces a greater and more lasting contraction than that from black ones. The eyes are probably endocrine organs producing a substance which brings about a contraction of the chromatophores. There is not any evidence to indicate that expansion of chromatophores is a result of tonus or deficiency of substance bringing about contraction.

WYMAN, Boston.

SOME ANATOMOPATHOLOGIC ASPECTS OF EXPERIMENTAL HERPETIC MYELITIS. ROBERT BING and BERN. WALTHARDT, Schweiz. Arch. f. Neurol. et de Psychiat. **22**:3, 1928.

Doerr and Voechting were the first to show that, in the rabbit, corneal inoculation with the contents of a herpetic vesicle would provoke not only the local reaction described by Grüter, but also a disease of the central nervous system which may be classed among the encephalitides. Walthard showed that when the content of an herpetic vesicle is inoculated into the hind paw of a rabbit after a blocking injury of the sciatic nerve, it will produce a local eruption of vesicles but no invasion of the central nervous system; on the other hand, an herpetic myelitis almost invariably appears when the sciatic nerve is not injured beforehand. The ascent of various toxins, such as rabies and tetanus, along the fibers of peripheral nerves has long been known, and in herpes one evidently has an infection which belongs to the same category.

There is some difference of opinion as to the precise route taken by the virus in the nerve. Marinesco and Draganesco believe that the ascent is by way of the perineural lymphatics. Goodpasture, Teaque and Pette believe that the virus ascends along the axis cylinders. Walthard's investigations led him to conclude that the invasion is perineural. He found an infiltration consisting chiefly of lymphocytes and a few polymorphonuclear leukocytes and desquamated endothelial cells in the perineurium. The perivascular spaces were particularly involved. The arterioles were found to be dilated and the cells of the sheath of Schwann showed proliferation. The axons themselves showed relatively little change. After the seventh day, these acute lesions subsided rapidly. The posterior root ganglia showed relatively little evidence of inflammation.

Changes in the spinal cord appeared on the sixth day after plantar inoculation, and were especially marked in the lumbar region. The meninges, the posterior columns and the posterior horns were particularly affected. By the seventh day, the inflammation took on the picture of a transverse myelitis. The perivascular spaces were crowded with lymphocytes and macrophages, the vessels were engorged, and small abscesses appeared. This process extended both caudad and cephalad; the intensity of the inflammation diminished, however, with increasing distance from the primary site. Both gray and white matter were involved. In some cases the inflammation extended as far as the bulb, but in only two animals were the cerebral hemispheres involved. All the lymphatic pathways and the central canal were utilized in the dissemination. A striking observation was the severe involvement of the cord as compared with the sciatic nerve. Degeneration could readily be demonstrated in the cord by the Marchi stain. The neuroglia tissue played relatively little part in the repair processes; on the other hand, the connective tissue was active in this respect, and massive mesodermal cicatrices appeared.

WOLTMAN, Rochester, Minn.

A CASE OF CHRONIC ENCEPHALITIS WITH MARKED INVOLVEMENT OF THE CORTEX. KONRAD ZUCKER, Ztschr. f. d. ges. Neurol. u. Psychiat. **113**:313 (March) 1928.

Cases of chronic encephalitis with particular implication of the cortex have been reported. Wilckens described three cases, one of which showed widespread involvement of the cerebral cortex as well as disease of the basal ganglia, such as is seen in encephalitis. The fifth cortical layer especially was involved, and the third layer was least involved. Marinesco and Baloi reported one case of enceph-

alitis showing disease of the cortex, especially in the insula and frontal lobe. Poppi, de Cresi, Buscaino and Agostine have reported similar cases. Scholz reported a case of encephalitis with involvement of the cortex in which mental symptoms were present, and in which the pathologic process spread in increasing intensity from the frontal lobe to the occipital lobe, where it reached its highest intensity. Zucker says that the cortical changes in chronic encephalitis never reach the intensity which they attain in the substantia nigra and other subcortical areas.

Zucker reports a case in a woman, aged 50, with typical paralysis agitans. Histologic study showed the most severe changes in the substantia nigra, then in the pallidum and thalamus, shading off to less severe changes in the neostriatum, cornu ammonis and pons. The cortex was everywhere involved, but was most markedly implicated in the postcentral region and the gyrus angularis. Less marked changes were present in the granular and agranular frontal areas and in the temporal areas. The frontal pole was slightly involved and the occipital area was least implicated. The olives, dentatum and spinal cord also showed changes in the form of degeneration. In all parts of the cortex there was a generalized glial proliferation and hypertrophy of all forms of glia. The Hortega microglia cells, in particular, were involved. They were increased in number, similar to the process in general paresis, but Zucker stated that the reaction was even more pronounced in this case of encephalitis than is usually seen in paresis. The macroglia showed definite perivascular proliferation. The basal ganglia were also markedly involved in the disease process in a manner similar to that already outlined. The ganglion cells of the cortex showed striking changes. The architecture was disarranged in several areas, especially in the gyrus angularis, the postcentral gyrus and in the lower layers of the agranular frontal region. While in all the frontal areas the third cortical layer was most markedly involved, in the angular, postcentral and first and second temporal gyri the most severe changes were in the lower layers and the less severe changes in layer three. In the postcentral gyrus, the fourth layer had practically disappeared. The ganglion cells showed similar changes everywhere—a large, swollen nucleus, a loss of Nissl granules and a homogeneous nucleus and cytoplasm. The cornu ammonis showed similar cell changes.

ALPERS, Philadelphia.

CONCERNING THE FUNDAMENTAL PATHOPHYSIOLOGIC MECHANISMS OF THE PSYCHONEUROSES. A. G. IWANOW-SMOLENSKY, Schweiz. Arch. f. Neurol. u. Psychiat. **22**:13, 1928.

In Pawlow's laboratory, special attention has been paid for some time to the so-called experimental neuroses in dogs. When positive and negative conditioned reflexes in animals become complicated, the equilibrium between the cerebral processes of excitation and inhibition becomes much disturbed. The behavior of the animal is completely changed. This disturbance, however, is temporary and usually subsides within a few weeks or months. During the period of disturbance the animal may become excited or inhibited, or both processes may alternate. It is interesting to note that these manifestations may not appear until the lapse of several days after the crucial experiment. In monkeys, the excitation is sometimes extreme; the animal may run about the cage, strike the breast with the fists, show the teeth, cry out and attempt to bite.

The investigation of forty-five neurotic patients showed that their ability to take on new automatic movements is disturbed. This hindrance also disappeared after their recovery. Two groups of neurotic patients could be distinguished: In the first, which comprised chiefly the traumatic neuroses, anxiety and compulsion neuroses, the positively conditioned reflex could be established only with the greatest difficulty. One of the best signs that a new reflex has become established is the shortening of the latent period to a definite interval. A lengthening of this latent period always shows activity of the inhibitory processes of the cortex. In the other group, comprised chiefly of hysterical patients, the conditioned reflexes

become established rapidly; however, only in a highly generalized form. For example, if a conditioned reflex is established for "do" of a certain octave, all other tones two or three octaves higher and lower will be followed by a reaction.

In some cases there is marked evidence of inhibition and in others of excitation. When the instinctive or chain reflexes come in conflict with an insurmountable obstacle, one may distinguish various types of neuroses, such as sexual neuroses, anxiety neuroses and occupational neuroses. A neurosis has its basis in the cerebral conflict between excitation and inhibition; this leads to a displacement of complexes. The ontogenetic ability of the hemispheres to adapt themselves to the environment is individual. One may assume that in the neuroses there is a relative insufficiency of bioadaptation. The more complicated the positive or negative environmental stimuli and the greater the disharmony of the inherited phylogenetic experience, the more easily and quickly does this cerebral inadequacy express itself in the form of some neurosis.

WOLTMAN, Rochester, Minn.

THE CEREBELLAR CORTEX IN DEMENTIA PARALYTICA FOLLOWING TREATMENT WITH MALARIA. C. TRÉTIAKOFF, Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **29**:1, 1927.

Trétiakoff examined histologically the cerebellums of five patients with general paralysis who died during a course of malarial treatment. Special attention was paid to the malarial pigment in the nerve tissues. The author had previously studied the accumulation of a peculiar pigment in the brain of a patient suffering from alcoholism and dementia who also had latent malaria. In this case small dark spots, widely and irregularly scattered over the cerebellar cortex, could be seen macroscopically; microscopically, these spots were fine, black granules of pigment scattered diffusely over and in the vessels and subarachnoid space, infiltrating also the cerebeller cortex, especially the larger Purkinje cells; here the infiltration was so extensive that even under low magnification and without staining they appeared as an uninterrupted new layer; the granules had been "phagocyted" by the glia cells, and appeared as fine dust within the protoplasm of the Purkinje cells.

In two of the five cases of general paralysis studied the cerebellar cortex showed numerous dark spots macroscopically, which on microscopic examination were found to consist of pigment in localizations similar to those observed in the case of alcoholic dementia. Except for this accumulation of pigment, the nerve tissue in the pigmented areas was apparently normal. However, there was unquestionably a general paralytic meningo-encephalitis with a certain degree of parenchymatous degeneration and a moderate degree of neuroglial proliferation. The Purkinje cells were normal, and there was little leukocytic infiltration in the nerve tissue and meninges.

Trétiakoff believes that the granules found in these cases are malarial pigment; its abundance in the vessels would seem to favor a hematogenous origin. The presence of malarial pigment in the central nervous system of persons who have succcumbed to malaria is not unusual, but it is difficult to explain the peculiar selective infiltration of the Purkinje cells. The author thinks that this may be due to the peculiar distribution of the blood vessels, because the capillary network in the layer of Purkinje cells is unusually rich. The deposition of the pigment in the Purkinje cells may be due to the special manner in which the latter receive their nutrition, as these cells are extremely poor in lipoid pigment.

KESCHNER, New York.

TRIGEMINAL NEURALGIA. FOURTEEN YEARS' EXPERIENCE WITH FRACTIONAL SECTION OF THE SENSORY ROOT AS THE MAJOR OPERATION. CHARLES H. FRAZIER, J. A. M. A. **89**:1742 (Nov. 19) 1927.

There are many angles and many aspects of tic douloureux that do not appear in current literature. The disease, while comparatively frequent in large neurosurgical clinics, is seen rarely by even the busiest practitioner. Contrary to what

might be expected, diagnosis is not always easy and many atypical cases are seen for which drainage of the antrum (maxillary), extraction of teeth and sometimes attempted injections of the sphenopalatine ganglion have been performed, without relief and perhaps with aggravation of symptoms. Frazier believes that the victims of trigeminal neuralgia are persons called highstrung. There are only two ways of affording relief for major trigeminal neuralgia. The patient should be informed of the limitations of alcoholic injection and of the enduring effect of the radical procedure, but he should be told that if the latter is chosen numbness will be present where there is pain.

Frazier not only again urges the adoption of his modification of the original Spiller operation (total section of the sensory root), which was subtotal section of the sensory root, but suggests a further application of the principle of fractional section of the sensory root. He offers embryologic and clinical defense for his principle of subtotal section with conservation of the ophthalmic division of the root. The two principle objections to the subtotal section, the difficulty of examination and the fear of recurrence, are discussed. Suggestions regarding the proper exposure of the root are given.

Frazier believes that the time has come for a wider application of his principle of subtotal section of the sensory root, and the underlying principle as he practices it today is that "there is no necessity for dividing more than that portion of the sensory root which supplies the portion of the gasserian ganglion and its corresponding division, through which the pain is referred." At the onset tic douloureux never involves more than one branch of a single division but later may spread to the entire division and then to the other divisions. When two divisions are affected, the one affected first is the first to show pain. In addition, when two divisions are involved alcoholic injection of the division first involved often controls the paroxysms in both.

The author urges unreservedly the conservation of the inner or ophthalmic portion of the nerve.

CHAMBERS, Syracuse, N. Y.

EPILEPTIC VARIANTS. S. A. KINNIER WILSON, J. Neurol. & Psychopath. **8**:223 (Jan.) 1928.

A large number of cases which present intimate or remote similarities to the phenomena of epilepsy as usually understood, but which do not seem to resemble each other, may be termed epileptic variants. Close study of these conditions is particularly fruitful in dispelling any idea of epilepsy as a self-contained and sharply dilimited clinical entity.

The clinical phenomena of epilepsy represent escape from physiologic inhibitions. It is immaterial whether they indicate only release or release and irritation, for if an irritative process is to exteriorize itself, it must succeed in overcoming inhibition. Epileptic possibilities are legion. No framework can be fashioned to embrace them all. Frontal, rolandic, parietal, occipital, temporal, mesencephalic, pontile, bulbar, cerebellar, and perhaps spinal epileptic syndromes, may be distinguished. Cannot similar physiologic processes conceivably affect visceral neural plexuses and ganglionic collections? The author considers "epilepsy of the solar plexus" a possibility. Common sense compels one, if one appropriates this wide conception of the condition, to speak of "the epilepsies" and to disabuse the mind of the idea that one and all must always display a somewhat forbidding aspect. In many instances one sees at a glance that the epilepsy is symptomatic. In so-called idiopathic or unknown epilepsy search should still be directed toward discovery of the underlying cause, which must exist. To establish standards of universal applicability, even in regard to the main classes of epilepsy, becomes a never ending task. The phenomena of the epilepsies edge off by easy gradations from the motor convulsive seizure to psychic, sensory or visceral symptoms of a highly disparate kind, and at the same time refuse to be separated for any physiologic reason. Under the head of "Motor Variants" the author lists myoclonic or regional epilepsy, epilepsia partialis continua, tonic epilepsy, coordinated epilepsy

and inhibitory or akinectic epilepsy. Under "Sensory Variants" there are reflex epilepsy, sensory epilepsy and affective epilepsy. Illustrative cases of each are presented. "Psychical Variants" and "Visceral Variants" are discussed. It is our task, with open mind, to observe symptoms, collect data, and collate instances, and imagination may supply the light whereby one will see eventually how heterogeneous syndromes slip into their places in the physiologic puzzle.

FAVILL, Chicago.

HEMIATROPHIA FACIEI DEXTRA FOLLOWING THYROIDECTOMY. PAUL MAUTHEY, Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:192 (April) 1928.

Mauthey reports a case of right facial hemiatrophy which developed six months after thyroidectomy. The hemiatrophy was typical, with atrophy of the skin, subcutaneous tissue, fat, facial and tongue musculature, changes in the hair and eyelashes, miosis, enophthalmos and ptosis, vasomotor changes, and anhidrosis in the right side of the face. It is postulated that in the thyroidectomy the cervical sympathetic nerve was injured causing the facial hemiatrophy. In 1,196 cases in which thyroidectomy was performed, Kaelin found the cervical sympathetic nerve injured in 12, but in none of these was there facial hemiatrophy. Others also have failed to report this condition following the cutting of the cervical sympathetic branch. Others have reported cases of hemiatrophy following trauma to the cervical sympathetic nerve, from pressure of an ossified lupoid (Mendel), from swelling of the thyroid, from adhesions of lymph nodes to the cervical ganglia, from pressure of a cervical rib, from adhesion of a cervical ganglion to the pleura, from apical tuberculosis with an adhesive pleurisy and finally from tumor of the third to the fifth cervical vertebrae. Oppenheim reported a typical case of facial hemiatrophy occurring after removal of a swollen lymph gland in the region of the superior cervical ganglion, with recovery.

All these observations support the view of Eulenberg, projected in 1875, that facial hemiatrophy is due to injury of the sympathetic nerve. In almost all his cases in which injuries to the cervical sympathetic nerve occurred Cassirer found some evidence of facial hemiatrophy. That in some cases of hemiatrophy there is anhidrosis, and in others hyperhidrosis is explained by the fact that in some cases the sympathetic fibers are irritated, while in others they are paralyzed. Other authors attribute facial hemiatrophy to injury of the trigeminal; Loeb, Mendel, and Wiesel reported an interstitial neuritis with loss of nerve fibers and cells. Still others consider this condition due to an injury of the vegetative fibers during their central course in the midbrain and in the walls of the third ventricle. Mauthey favors injury to the cervical sympathetic nerve as a cause of facial hemiatrophy.

ALPERS, Philadelphia.

THE BLOOD VESSELS OF ANNELIDS. HENRY FEDERIGHI, J. Exper. Zool. **50**:257 (Feb. 5) 1928.

The vascular system of *Nereis virens* consists of a contractile dorsal vessel and a noncontractile ventral vessel. These are connected in each segment by a series of lateral branches which are contractile. Four distinct layers are found in the blood vessels. These layers are an innermost continuous endothelium, a continuous homogeneous cuticula, the "adventitia" and, outside of all, a discontinuous peritoneal layer. These layers vary in different types of vessels. The "adventitia" may vary in structure from isolated stellate cells to almost typical smooth-muscle cells ("Muskelzellen"). These cells, however, never form a continuous layer, nor do their branches anastomose. A comparison of the vertebrate capillary and the annelid blood vessel shows that both types of vessels possess an inner endothelium, and an outer, histologically somewhat similar, "adventitia" (in vertebrates the "Rouget" cells).

The normal contraction wave in the contractile vessels of *Nereis virens* is independent of any central nervous system control. Two types of contraction

can be seen, a normal contraction wave of a peristaltic character and local contraction produced only on direct stimulation. The normal contraction wave is due to the independent active contraction of the endothelium. Local constriction depends on the contractility of the "Muskelzellen." These appear to be capable of active contraction only on direct stimulation. Their function may be to prevent excessive bleeding following the cutting of a vessel. A comparative study of the vertebrate capillary and the annelid blood vessel reveals the fact that the normal contraction in both types of vessels depends on the independent contraction of the endothelium. It seems probable that the "Rouget" cells are functionally analogous to the "Muskelzellen."

WYMAN, Boston.

PAROXYSMAL HYPERTENSION WITH TUMOR OF RETROPERITONEAL NERVE: REPORT OF CASE. CHARLES H. MAYO, J. A. M. A. **89**:1047 (Sept. 24) 1927.

The ultimate condition in hypertension is accepted as being due to reduced cross-section of the arteriolar tree. The Leriche operation and the more recent lumbar and cervical sympathectomy have taught much as to the sympathetic control of the circulation in the extremities. Mayo presents a case of paroxysmal hypertension which is interesting because of an unusual history, difficulty in diagnosis and the complete and permanent relief obtained by the removal of a tumor, apparently the inciting cause of the hypertension. The essential features of the case are as follows:

A woman, aged 30, had been ill for a year and a half prior to coming to the clinic. For the last few weeks prior to admission she had been incapacitated for work and had suffered from paroxysmal attacks of precordial discomfort, occipital headache, pallor, cold, clammy skin and a peculiar choking sensation followed by nausea and vomiting. Cough occurred frequently during the attack, with expectoration of frothy, frequently blood-tinged saliva. There was considerable abdominal distress on the right side. During these attacks tachycardia was present which was, however, secondary to a high blood pressure, the pressure going from 120 or 130 to 280 or 320 mm. or more, while the diastolic increased from 80 or 90 to 160 or 180 mm. Abdominal distress and the belief that there might be an involvement of the abdominal sympathetics led to exploration, and a tumor over the left suprarenal and beneath the tail of the pancreas was found and removed. It proved to be nerve tissue. The pathologic diagnosis was retroperitoneal malignant blastoma. Reports of four cases of paroxysmal hypertension were gleaned from the literature. A diagrammatic sketch showing the location of the tumor, a photograph of the tumor and a photomicrograph of its histologic structure are presented.

CHAMBERS, Syracuse, N. Y.

FETISHISM. SIGMUND FREUD, Internat. J. Psycho-Analysis **9**:163 (April) 1928.

Freud states that the devotees of fetishes regard them as abnormalities but only rarely as symptoms of illness. As a result of accumulated analytic experience, Freud has come to the conclusion that the fetish is a substitute for the penis —not a substitute for any chance penis but for the woman's (mother's phallus), which the little boy once believed in and does not wish to forego. This perception has persisted, and the fetishist has exerted an energetic action to keep up his denial of it. He retains the belief unconsciously, but he also gives it up, and during the conflict a compromise is constructed such as is possible only in the realms of unconscious modes of thought. Aversion for the real female genitals, which is never lacking in any fetishist, also remains as an indelible stigma of the repression of the female phallus image which is taking place. The adoption of the fetish saves the fetishist from being homosexual by endowing women with the attribute which makes them acceptable as sexual objects.

Freud has observed that tender and hostile treatment of fetishes is mixed in unequal degrees analogous to the denial and at the same time recognition of castration. He believes that pathologic instances in which the compulsion exists to cut off woman's plaits of hair depends on the impulse to execute symbolically the

castration which the person denies. Freud closes his contribution with the statement that "normal prototype of all fetishes is the penis of the man — just as normal prototype of an organ felt to be inferior is the real, little penis of the woman, the clitoris."

My own clinical experience would seem to corroborate Freud's theory. While I have treated numerous cases in men in which fixation on a fetish such as shoes, arm-pits, forearm, played an important rôle, I do not recall a single case of fetishism among women patients, although, roughly speaking, my clinical material has been equally divided between the two sexes.

OBERNDORF, New York.

THE ALBUMOSES AND THEIR RELATION TO EPILEPTIC AND INSULIN CRISIS. GEROLAMO CUNEO, Biochim. e terap. sper. anno dodicesimo, fascicolo terzo, 1926.

The author, after an exhaustive investigation, observes that the albumoses found in epileptic patients behave like insulin. When injected into the veins of dogs, they produce convulsions, lowering the blood sugar as low as from 0.5 to 0.4 per thousand, precisely as happens with convulsions induced by insulin. He finds similar hypoglycemia in epileptic patients just before or during the convulsive seizure, and injections of dextrose have produced a complete suppression of the attacks. He is inclined to think that insulin is an albumose or a substance analogous to albumose.

When the albumoses are precipitated they assume either a waxy or a flocculent form. The waxy precipitation produces convulsions and lowers the blood sugar as low as from 0.5 to 0.4 per thousand. The flocculent precipitant does not produce convulsions, and the glycemia is never below 0.57 per thousand; it causes only toxic phenomena. These toxic symptoms correspond to those found in certain epileptic patients without convulsive seizures.

When subcutaneous (and, as Dr. Osnato has found, intravenous injections of from 10 to 15 per cent) injections of 10 per cent dextrose were administered to twenty patients with daily epileptic seizures, the attacks were suppressed for twenty-six days. After this time, three patients had a remission of the convulsions, while a few others experienced milder attacks.

Analogous action was observed between injections of insulin and dextrose not only in rabbits but in diabetic patients.

The author finds that injections of dextrose suppress epileptic convulsions in the same manner that the convulsions produced by the albumoses and insulin are suppressed.

VINCIGUERRA, Elizabeth, N. J.

THE FINER ANATOMY OF VERTEBRAL AND PARAVERTEBRAL SYMPATHETIC GANGLIA IN THE SIMIANS. F. DE CASTRO, Arch. de neurobiol. **7:38** (Jan.-Feb.) 1927.

The article reports a detailed study of the structure of the superior cervical, stellate, thoracic and semilunar ganglia of the monkey (*Macacus sylvanus*). Cajal's reduced silver nitrate method was used for the preparation of the slides.

In the superior cervical ganglion there exist sensory cells that have migrated from the nodose ganglion of the vagus, and in some places both sensory and sympathetic elements appear mixed. From about one half to one third of the upper third of the ganglion is occupied by the large monopolar neurons of the nodose ganglion, with their thick axons, while the rest of the ganglion shows finer fibers and smaller, multipolar sympathetic neurons. A few of the monopolar neurons of the vagus are embedded in the sympathetic portion. Similar conditions were described by Dogiel in the nodose ganglion of the cat, and by the author in man.

The sympathetic ganglia of the monkey must be regarded as a link between the ganglia of the large mammals (cow, sheep, goat) and the ganglia of man. The most frequent cell types in the monkey are: (1) Neurons with long dendrites,

present in all the sympathetic ganglia; (2) fenestrated neurons, not so complex as the corresponding elements of the ruminants, especially the bovidae; (3) cells with short and long dendrons, the former abundant, in which respect the monkey closely resembles man in whom short dendrons are numerous; (4) neurons with dendritic glomeruli. These are common in the cervical ganglia. The monocellular type is the most frequent, but there are also bicellular and tricellular glomeruli.

The synapse of the sympathetic cells and the preganglionic fibers is also described.

NONIDEZ, New York.

ON THE PATHOLOGY AND LABORATORY DIAGNOSIS OF PARESIS. FREDERICK PROESCHER and ALBERT ARKUSH, J. Nerv. & Ment. Dis. **67**:21 (Jan.) 1928.

The authors discuss briefly the literature on the distribution of the iron pigment in general paralysis and particularly the ideas of Spatz and the relationship between the glia and the iron deposits. Their previous studies on the brains of patients with general paralysis with their improved method of staining with thiozin red tend to support the view that the iron deposits in general paralysis are of an inorganic and not of an organic nature. The large iron containing phagocyte or Hortega cells in the brain float free from the vessel wall into the perivascular lymph space and thence find their way into the spinal fluid. These adventitial cells may then be stained in the spinal fluid by any stain for inorganic iron.

They advise the following procedure: from 5 to 10 cc. of spinal fluid is withdrawn and centrifugalized. To the sediment is added 5 cc. of an alcoholic ammonium hydroxide sulphide solution made as follows: 95 cc. of 96 per cent alcohol is added to 5 cc. of an aqueous solution of ammonium hydroxide. The spinal fluid with the reagent is then centrifugalized, and a few drops of the sediment are examined on a slide under a cover glass. The pigment in a positive case must exist within the adventitial cells, which appear large, irregular and refractile. The pigment granules are deep black, angular, rounded or spirene.

The test seems specific for general paralysis, being absent in fluids from dementia praecox, manic-depressive, epileptic, arteriosclerotic and senile patients. The stage of the disease influenced the intensity of the reaction.

FERGUSON, Upper Darby, Pa.

SENSORIAL APPERCEPTION AND INTERNAL APPERCEPTION. L. LEY, J. d. neurol. et d. psychiat. **27**:147 (March) 1927.

Apperception, according to Leibnitz, is a psychic activity which modifies, elaborates and coordinates the perceptions arising from the external senses or from the intimate sense, and integrates them to the content of the soul or to the previous acquisitions of the mind. Apperception is then considered as a spontaneous, conscious activity. Apperception may be divided into an external apperception, or sensorial, and internal apperception, intellectual or psychic. It consists mainly in the fixation by means of the attention of a sensorial stimulus or of an idea or image into the center of consciousness.

Dissociation between internal and external or sensorial apperception may be found in some demented or confused patients. Sensorial as well as psychic apperception persists at times in an astonishing manner in some demented persons showing a global mental defect (general paralysis, organic dementia). The persistence of apperception in such severe forms of dementia contradicts the psychologic conception by which apperception is considered to be the substratum of the whole superior mental life. We do possess, according to Janet and Hoffding, a superior mental synthetic activity which acts automatically as an original and specific function independently from apperception and which may disappear following an organic brain disease, while the apperception may still be preserved.

FERRARO, New York.

ON PALILALIA. MACDONALD CRITCHLEY, J. Neurol. & Psychopath. **8**:23 (July) 1927.

Palilalia is a variety of reiteration; the patient repeats many times a word, phrase or sentence which he has just spoken. The tendency is to speak more and more quickly and with less distinctness until speech becomes almost inaudible. The patient is aware of the defect but can seldom control it. Seven cases are presented, four being postencephalitic and three cerebral arteriopathic. This symptom disappears during reading out loud, singing, or reciting from memory. Evidence of repetitions of writing or repetitions of movements executed by the patient himself have never been found. Aphasia, in the accepted sense of the word, does not occur. Disturbances of emotivity and intellectual impairment are frequent accompaniments. Parkinsonism is always the underlying feature in the postencephalitic cases, while pseudobulbar syndromes are commonest in the arterial group. Localization is most difficult and, on the basis of one of his arterial cases which came to postmortem examination and of a review of published cases, the author thinks that palilalia is the expression of a diffuse morbid process or of the summation of numerous isolated lesions. This is a disorder of speaking, not of speech, since internal speech is normal and the trouble is purely in the effector mechanism. In both parkinsonism and pseudobulbar palsy, reduction of volitional activity occurs. Analogy is made with the act of walking; this is hard to initiate but when started is often hard to stop. Thus, in palilalia it is easier for the patient to go on talking than it is to cease.

FAVILL, Chicago.

CEREBROSPINAL FLUID IN NEPHRITIS. JOHN D. LYTTLE and LESTER ROSENBERG; assisted by JOHN HEARN, Arch. Int. Med. **39**:808 (June) 1927.

The authors studied the cerebrospinal fluids of the patients in twenty-two cases of nephritis, comparing the percentage of constituents with that in the blood. The results were: The fluid was clear and had a cell count varying from two to sixteen cells, practically all being lymphocytes. The nonprotein nitrogen of the spinal fluid was increased and was higher than the normal proportion in relation to the blood content. The usual ratio of cerebrospinal fluid nonprotein nitrogen to blood nonprotein nitrogen, normally 46 per cent, rose to 80 per cent in the presence of nitrogenous retention. The chlorides were not generally increased, nor did this vary in the presence of edema. There was a definite increase in albumin and globulin, with the highest figures occurring in nephritis. When the protein surpassed 100 mg. per hundred cubic centimeters, the prognosis was grave. The ratio of blood sugar to cerebrospinal fluid sugar was higher in nephritis, averaging 74.3 in eleven cases. These figures were higher in the presence of uremia. In the absence of symptoms of uremia in acute nephritis the cerebrospinal fluid was essentially normal; when uremic symptoms occurred, the protein content was higher. There was no characteristic change in the colloidal gold curve in nephritis.

ANDERSON, Philadelphia.

CONVALESCENT SERUM IN EPIDEMIC POLIOMYELITIS. EDITORIAL, J. A. M. A. **91**:398 (Aug. 11) 1928.

The great importance of diagnosis of the preparalytic stage of poliomyelitis, when it may be possible to neutralize the virus before it can produce its maximum destructive effects on the motor nerve cells, is again emphasized. A résumé of the symptom picture as given by Aycock and Luther is presented. Prostration is out of proportion to a temperature usually under 102 F. The face is flushed, the expression is anxious and there is frequently pallor about the nose and mouth. The pulse is rapid. There may be a coarse tremor on motion. There is a distinct cervical rigidity but not as marked as the type seen in meningitis. A characteristic stiffness of the spine is present. The deep reflexes are usually hyperactive at

this stage. Lumbar puncture should be done and yields a fluid under moderately increased pressure, clear on gross examination but hazy to transmitted light; the number of cells varies from 20 to 800 (average 50 to 250); early in the condition the cells may be polymorphonuclears, but later are lymphocytes. Globulin is increased. The favorable results of Aycock and Luther and theoretical considerations justify the use of convalescent serum. Flexner and Stewart suggest its possible use for preventive purposes.

CHAMBERS, Syracuse, N. Y.

MALARIA THERAPY IN THE VIENNA PSYCHIATRIC CLINIC. JULIUS VON WAGNER-JAUREGG, Wien. klin. Wchnschr. **40**:1121-1122 (Sept. 8) 1927.

In the ten years that malarial therapy has been employed by von Wagner-Jauregg, patients with all types of general paralysis have been treated; but he has come to the conclusion, however, that two types of the disease should not be subjected to this method of therapy: the so-called galloping general paralysis and the late forms with extreme physical disability. Fatalitis have almost disappeared. Eight malarial injections are now the rule, although each case merits careful consideration and a rigid program is not maintained. The injections are stopped for a time and neoarsphenamine is used in patients who react poorly. Later the malarial treatments are again resumed. During the early period of malarial treatment it has been found that the spinal fluid cannot be considered as an index of the value of the treatment. Later, the fluid may become entirely negative and it is in these cases that the prognosis is, as a rule, satisfactory. It is customary in his clinic to follow the malarial treatment with neoarsphenamine.

MOERSCH, Rochester, Minn.

SYPHILIS AND EPILEPSY. HAROLD A. PATTERSON, Am. J. Syph. **12**:41 (Jan.) 1928.

From a study of his own cases the author believes the following conclusions are justified: 1. In a group of forty-one epileptic patients with syphilis, the syphilis appeared much more frequently as an incidental than as an etiologic factor. 2. In those instances in which it did assume a causal rôle, the syphilis preceded the epilepsy; in those instances in which it seemed to occur as an incidental element, the syphilis was, as far as could be ascertained, likely to run its course independently of the epilepsy. 3. In those cases in which it may have been etiologic, antisyphilitic treatment seemed decidedly beneficial in ameliorating the resulting convulsive disorder. 4. When it was coincidental the effect of antisyphilitic treatment was dubious.

An analysis of the literature and of his own cases, in an epileptic colony, appears to point to the conclusion that the incidence of syphilis in epilepsy is less frequent than among the insane or the feebleminded, and that its occurrence probably does not exceed the rate obtained among the population as a whole.

ANDERSON, Philadelphia.

THE FATE AND DEVELOPMENT OF THE IMMATURE AND OF THE PREMATURE CHILD: PART I. AARON CAPPER, Am. J. Dis. Child. **35**:262 (Feb.) 1928.

The first article of this study includes a review of the literature of cerebral hemorrhage in the new-born infant. Clinical and pathologic data are presented to show the enormous frequency of cerebral injury at birth. Authority is quoted to show that cerebral trauma at birth causes a loss of human life so great that it may be considered as one of the most widely spread diseases. Next to tuberculosis, disease of the nervous system due to cerebral trauma at birth is the most widely prevalent disease, and its mortality rate is one of the greatest. Ten per cent of all new-born infants who died at the end of the first month suffered from cerebral trauma. This great loss of human life is overwhelmingly caused by the traumatic injury of the brain at birth; all

other causes — congenital syphilis, asphyxia due to cord around the neck, asphyxia through anomalies of the delivery, primary infections and malformations — are present in a small number of cases when compared with the number in which trauma is the cause.

VONDERHE.

ON THE TRAUMATIC DEVELOPMENT OF PARALYSIS AGITANS. F. LOTMAR, Der Nervenarzt. **7**:16, 1928.

While the relation of trauma to such maladies as syringomyelia, tabes and multiple sclerosis often has come up for discussion, little has been said concerning this relationship in paralysis agitans. The author, therefore, cites two cases bearing in some degree on this question. The first patient was a healthy man, aged 31, who, shortly after being thrown on his back, developed a paralysis agitans syndrome. After three years this had progressed little; but a second injury, four years after the first, evoked an almost immediate exacerbation of the illness. The second case was that of a healthy man, aged 43, who rapidly developed symptoms of this character following an injury to the back. In this instance the trouble was chiefly manifest in the legs.

His conclusions are that there is a traumatic paralysis agitans in the sense that, in a completely healthy young person, a sudden injury or shock can forthwith be followed by the appearance of this type of symptoms. The special circumstances which produce these results are, of course, yet unknown.

ANDERSON, Philadelphia.

STUDIES IN ANIMAL AGGREGATIONS: MASS PROTECTION FROM FRESH WATER FOR PROCERODES, A MARINE TURBELLARIAN. W. C. ALLEE, J. Exper. Zool. **50**:295 (Feb. 5) 1928.

Procerodes wheatlandi, a marine turbellarian, survives exposure to equal amounts of tapwater for a longer time if numbers of the species are present. The protection may be due, in part, to the increased salinity furnished by the greater numbers of worms. Marked protection is furnished worms isolated into 0.5 per cent seawater, while 2 per cent seawater solutions gave protection comparable with that furnished by bunch-conditioned tapwater. Numbers of well washed *Procerodes* kept in tapwater until the majority are dead condition the water so that fresh worms isolated into it may live markedly longer than do similar worms isolated into water with the same salt content. This protection was furnished by filtered water from the dead bunches, or by washed dead worms added to fresh tapwater. The filtrate retained its protective power after being brought to a boil. Water from living worms only, while protective, was less so than that in which worms had died and disintegrated.

WYMAN, Boston.

SYNREFLEXIA. A. AUSTREGESILO, J. Nerv. & Ment. Dis. **68**:1 (July) 1928.

Sherrington, Dejerine, Benedict and others have described association of reflexes, of which the author distinguishes the following types: (*a*) superficial reflexes with superficial; (*b*) superficial reflexes with deep reflexes; (*c*) superficial reflexes with visceral reflexes; (*d*) visceral reflexes with deep reflexes; (*e*) alternation of the three varieties. By stroking the under part of the arch of the right foot, the author obtained in a certain case a plantar reflex on the opposite side, and this exemplifies the superficial heterolateral reflex. Three factors may be said to produce the reaction: (1) the anatomic element formed by the complex reflex arc; (2) the physiologic element represented by the intensity of the initial excitement; (3) the pathologic element of increased intensity of response. The stimuli capable of producing the hyperreflexia can facilitate the appearance of associated reflexes. The author considers that synreflexia is a frequent phenomenon clinically. It is associated with hyperreflexia and interruption and deviation of paths of conduction. It may be regarded as bearing the same relation to the individual reflexes as synkinesia does to individual movements.

HART, Greenwich, Conn.

A Clinical Analysis of an Extrapyramidal Syndrome; Paralysis Agitans and Postencephalitic Parkinsonism. A. W. Young, J. Neurol. & Psychopath. **8**:9 (July) 1927.

The author has carefully analyzed fifty cases, thirty-nine of which were of postencephalitic parkinsonism and eleven of the idiopathic type of this disease. Among the various points brought out, the following are of special interest: The average interval between an attack of encephalitis and the onset of parkinsonian symptoms was 7.2 months. The average duration of parkinsonism in postencephalitic cases was 2 years and 2 months.

Items especially analyzed are speech, movements of cooperation, associated movements, simple and combined movements, general motility and tremor. A comparison of the symptomatology of postencephalitic and idiopathic cases shows definite distinctions. In the former, stiffness and sialorrhea occur more often. In the latter, tremor and "weakness" are more frequent. Disturbances of pupillary reactions and movements of the tongue are more common in postencephalitic cases. The author finds that associated movements are not absent in parkinsonism.

Favill, Chicago.

A Case of Complete Absence (Congenital) of Both Upper Extremities. Alfred Strauss, J. f. Psychol. u. Neurol. **36**:75, 1928.

The subject was an 8 months fetus that died of bronchitis at the age of 10 weeks. The fetus was 47 cm. long and weighed 2,320 Gm. The scapulas, acromion and clavicles, with their muscles, were the only parts of the upper extremities to be seen. Macroscopically there was nothing unusual about the cord or roots. Histologic examination showed: relative increase of the gray substance with failure of development of the motor region in the cervical and dorsal segments; diminution of the number of motor ganglion cells; irregular arrangement of these cells; dysplasia of the gray commissure; heterotopy of the white substance; double central canal. The arrangement of the anterior horns in the segments from the fifth cervical to the first dorsal segments did not differ from that of the dorsal cord, and there was no diminution in the size of the tracts or of the root fibers. From a study of the microscopic sections the author believes that in all probability the defect in the cervical cord began so early in the developmental stage that in the course of ontogenesis it was well compensated for; on the other hand, owing to the poor development also of the entire dorsal region of the cord, the hypoplasia of the cervical cord was less striking.

Keschner, New York.

The Kahn Test on Spinal Fluid. Thos. G. Hull, Louella Fay and Chester Garwood, Am. J. Syph. **12**:104 (Jan.) 1928.

Of 1,200 patients in whom Kahn tests were made on spinal fluids, clinical histories were obtainable in 410; of this number, 181 were diagnosed as syphilitic and 229 were diagnosed as nonsyphilitic. Of the 181 specimens from patients with syphilis, 135 gave positive Kahn reactions and forty-five gave negative reactions. All but fourteen of these negative reactions were from patients known to have received antisyphilitic treatment. In ten instances in which the colloidal gold test was made, and in nine in which the globulin test was performed, the results corroborated the negative Kahn reactions. Hence, it is believed that a high degree of specificity obtains in this test. Of the 229 cases of a clinically nonsyphilitic nature, seven showed some degree of reaction to the Kahn test; two of these were confirmed by the colloidal gold curves, and the others had varying degrees of corroboration from globulin and gold tests.

Anderson, Philadelphia.

PSYCHOGENIC FACTORS IN THE SEQUELAE OF CEREBRAL TRAUMA. GERALD PEARSON, J. Nerv. & Ment. Dis. **67**:449 (May) 1928.

Adolf Meyer, in 1904, pointed out that injuries to the brain, instead of causing changed personality, simply accentuated preexisting traits, and that the emotional consequences — fright and worry — of the injury must be considered of equal etiologic importance with the actual injury of the brain. The author presents two children who showed changes in behavior following injury of the head; in the first case, the trauma was the only concurrent, precipitating factor in the personality change; in the second, it produced some degree of security for the patient in his family circle, and the need for his overt misbehavior ceased. In both patients, the trauma caused regression to a former period of years. The headache and fatigability were a recrudescence of the symptoms suffered at that time. As this former illness occurred in infancy, many of the behavior reactions, e. g., the restlessness, were those of that period of life. In neither patient can any organic damage to the nervous system be held responsible for the symptom complex. These two cases show the necessity of a careful psychiatric study in cases of injury of the head in children as well as, in certain particulars, a study of some of the mechanisms of the development of adult psychoneurotic symptoms.

HART, Greenwich, Conn.

HEMIHYPERTROPHY. B. L. MCFARLAND, Brit. M. J. **1**:345 (March 3) 1928.

The patient, a boy, aged 12, had a short left leg and complained at times of pain in the right one. There had been a suspicion of inequality at the age of 3 weeks, and shortening of the left leg was definitely noticed when he started to school at the age of 5 years. For the five years previous to the time when he was seen, he had intermittent attacks of intense edema of the right leg, extending to the top of the thigh. These started with pain in the groin and were accompanied by anorexia, pyrexia and signs indicating toxemia. Pain was intense. The face and left arm were also swollen. The attacks occurred irregularly and lasted from ten to fourteen days. The right side of the body was larger than the left and this was most marked in the leg. The right leg was 2 inches (5 cm.) longer than the left, the calf 2 inches greater in circumference and the thigh 1½ inches (3.81 cm.) greater. The author thinks that the condition was due to a diffuse unilateral lymphatic or reticulo-endothelial hypertrophy. The attacks would then correspond to the intermittent inflammation which occurs in other lymphatic over-growth, such as cystic hygroma.

PETERSEN, Montreal.

TREATMENT OF PAINFUL CYSTITIS IN THE CYSTALGIC STAGE BY RESECTION OF THE PRESACRAL NERVE. CHARLES VIANNY, Arch. franco-belges de chir. **30**:229, 1928.

The syndrome of cystalgia resulting from chronic cystitis has been recognized for many years, and at the same time its rebelliousness to all forms of treatment. It has been determined that the inflammation of the bladder has spread to the nerve trunks, giving rise to a fibrous perineuritis which is probably responsible for the pain. Even as far back as 1903, Rochet had practiced resection of the perineal branch of the internal pudic nerve. However, intervention on the sympathetic system seems to offer even greater hope, especially since Leriche has obtained such good results in kraurosis vulvae. The section of the presacral nerve in this condition has given exceptionally good results since it does not interfere at all with the function of the bladder and yet it does away with the pain. Its simplicity is also something to recommend it.

FREEMAN, Washington, D. C.

SYNDROME OF CLAUDE BERNARD HORNER SUCCESSIVELY BILATERAL AND TRANSITORY. M. FROGÉ, Ann. d'ocul. ??:266 (April) 1928.

A patient who presented the syndrome of Claude Bernard Horner is reported by Frogé as of interest owing to the fact that it rapidly changed from the right to

the left side, although it was more marked on the left. The ocular symptoms improved, but the associated symptoms of pain and vascular involvement, including some burning and congestion, although they were slightly diminished, continued in the form of acute attacks. These cases are rare, although a previous instance in a pregnant woman was reported by Terrien. It is difficult to maintain that the symptoms were due to pregnancy, as they were aggravated after delivery. Endocrine treatment was unavailing, and removal of adenoid tissue resulted in only slight improvement.

BERENS, New York.

TREATMENT OF EPILEPTIC PERSONS WITH INJECTIONS OF AN EMULSION OF CEREBRAL SUBSTANCE IN SOLUTION OF SODIUM PHENOBARBITAL. R. NOVOA SANTOS, Arch. de neurobiol. **7**:213 (Sept.-Oct.) 1927.

The author has used an emulsion of cerebral substance in a 20 per cent solution of sodium phenobarbital; the dose injected was 2 cc. every other day until ten injections had been made. Extraordinary improvement, persisting for some time after the injections were discontinued, was observed in nine patients in whom the usual treatment was not successful, but the author cannot state how long the beneficial effects of the injections lasted, since the patients were discharged or were not kept under continuous observation.

NONIDEZ, New York.

FACIAL DIPLEGIA IN POLYNEURITIS OF A DIPHTHERIA CARRIER. PETER KÖNIG, Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:200 (April) 1928.

König reports a case of polyneuritis in a woman, aged 48, with a sudden onset of paraplegia, pains and paresthesia in the legs, and mild pareses in the fingers; the next night after the onset there was a bilateral facial paralysis. This was of peripheral type with electric reactions of degeneration. Cultures of diphtheria bacilli were obtained from the pharynx and tonsils. After two injections of serum, all the symptoms disappeared. König reports the case because the occurrence of polyneuritis in a carrier is unique and because facial diplegia in diphtheria is rare.

ALPERS, Philadelphia.

TOTAL OPHTHALMOPLEGIA OF THE LEFT EYE PROBABLY OF TUBERCULOUS ORIGIN. MONTHIS and CADILLAC, Ann. d'ocul. **165**:270 (April) 1928.

The case of a man, aged 24, is reported because he presented total ophthalmoplegia of the left eye and headaches both day and night. The results of a general physical examination were negative, except for an abscess in the groin. The results of physiologic tests were also negative. Specific treatment was not well borne. Inoculation of the pus into a guinea-pig showed the tuberculous nature of the lesion. The authors considered that the ophthalmoplegia probably was due to tuberculosis, although the location of the lesion was undetermined.

BERENS, New York.

PSYCHOSIS AND HYPERTHYROIDISM. W. O. JOHNSTON, J. Nerv. & Ment. Dis. **67**:558 (June) 1928.

This article is based on twenty-four cases of true psychosis occurring among 2,286 cases of operative goiter in the Cleveland Clinical Hospital in one year. The author regards operative results in any case showing a psychosis or delirium as uniformly unsatisfactory. With a psychotic family history, one can expect practically no improvement with treatment; the disease is usually fatal. Hallucinations and delusions with depressive states are the most characteristic symptoms. Even in the manic states, improvement is uncertain, and death from acute exhaustion may follow a recurrence of the excitement. The number of psychotic cases shows the relative rarity of psychoses in association with hyperthyroidism. The psychosis is aggravated by the hyperthyroidism and is not the result of it.

HART, Greenwich, Conn.

TITRIMETRIC QUINHYDRONE ELECTRODES: A COMPARISON WITH THE HYDROGEN ELECTRODE FOR HYDRION CONCENTRATION DETERMINATIONS IN PLASMA, WHOLE BLOOD AND OTHER BIOLOGICAL FLUIDS. GEORGE H. MEEKER and JOHN G. REINHOLD, J. Biol. Chem. **77**:505, 1928.

Using the titrimetric quinhydrone electrode, satisfactory agreement with the hydrogen electrode was obtained by Meeker and Reinhold on human serum, plasma and cerebrospinal fluid, as well as on various other biologic fluids. This electrode, however, was not satisfactory for whole blood or for the serums of dogs.

FREMONT-SMITH, Boston.

PSYCHIC FACTORS IN GENERAL DISEASE. EDITORIAL, J. A. M. A. **89**:1063 (Sept. 24) 1927.

The appreciation of the influence of mind over matter is as old as humanity, but the activities of charlatans has discredited attention given to the psychic element in visceral and somatic disorders. There are physicians, who, influenced by the comparatively recently acquired knowledge of tissue pathology, exclude the word "neurosis" and if no pathologic condition can be found, remain inactive as therapeutists, although their honesty and scientific spirit are laudable.

CHAMBERS, Syracuse, N. Y.

A NEW BLOOD SUGAR METHOD. OTTO FOLIN, J. Biol. Chem. **77**:421, 1928.

Folin describes a new and simple method for determining the sugar of the blood that requires the use only of 0.1 cc. of blood. An anticoagulant is not necessary. Values obtained by the new method are usually from 5 to 20 mg. per hundred cubic centimeters lower than by the Folin-Wu method.

FREMONT-SMITH, Boston.

BITEMPORAL HEMIANOPIA AS A RESULT OF FRACTURE OF THE SKULL. OKINCZYC and RENARD, Ann. d'ocul. **165**:270 (April) 1928.

A case is reported in which fracture of the skull produced bitemporal hemianopia, optic atrophy and loss of vision, and finally resulted in almost absolute paralysis of the right third nerve. The lesion seemed to be due to compression by a hematoma; since it was apparently retrochiasmatic, the isolated involvement of the third nerve can be explained.

BERENS, New York.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Regular Meeting, May 8, 1928

WALTER M. KRAUS, M.D., *President, in the Chair*

CASE REPORT ILLUSTRATING THE EARLY DIAGNOSTIC SIGNIFICANCE OF THE ENCEPHALOGRAM. By DR. E. D. FRIEDMAN.

Clinical History.—P. B., a farmhand, born in Russia, aged 36, single, was first admitted to the neurologic service of Bellevue Hospital on July 13, 1927, complaining of headache, pain over the entire right side, dizziness, especially following forced defecation, "lights before his eyes," pain behind the ears, especially in the morning, and generalized convulsions. The last had occurred at irregular intervals for one and a half years prior to admission. The family history was unimportant. The man had served in the Russian army during the World War and had been gassed. He contracted gonorrhea in 1917, and suffered from right-sided pleurisy In 1918. Tonsillectomy was performed in 1923.

Examination.—Physical examination revealed good pupillary reactions, normal fundi and no defects of the visual field. There was a slight right facial weakness with widening of the palpebral fissure. The abdominal reflexes were diminished on the right, and the right plantar response was equivocal. The right corneal reflex was diminished. Pinprick was perceived better on the left, and the patient complained of subjective pain on the right. There were no other sensory changes. Aphasia had not occurred.

The spinal fluid was clear, colorless and aside from the presence of 54 cells per cubic millimeter revealed no abnormalities. Results of Wassermann tests of the spinal fluid and the blood were negative. The cerebrospinal fluid pressure was 420 mm.

The general medical status proved normal. Results of the roentgen-ray examination of the chest were negative. The urine was normal except for a faint trace of albumin. Blood pressure readings were 138 systolic and 84 diastolic.

Diagnosis.—A focal lesion in the left hemisphere was the diagnosis. Encephalography was suggested in order to determine the nature of the lesion.

Encephalography.—Lumbar insufflation of air was carried out on Aug. 7, 1927. The encephalogram revealed a shifting of the ventricular system to the right. The anterior horn of the left ventricle was narrowed. The third ventricle was obliquely displaced to the right, and the anterior horn of the right lateral ventricle was somewhat dilated. The encephalographic appearance was that of left cerebral neoplasm.

Course.—The patient left the hospital at his own request.

He was readmitted on Dec. 28, 1927. His chief complaints at this time were, recurring fits, loss of strength and impairment of "memory." He still spoke of bright colors before the eyes just before the convulsive seizures, which recurred about once a week. These attacks seemed to be provoked by loud noises (acousticomotor reaction), and were followed by persistent dull pain over the entire right side. Members of his family observed a notable impairment of memory and a marked slowing of cerebration. He did not seem to understand spoken words as well as he had previously; this was especially true of conversation in English (his more recently acquired language).

Physical examination revealed no impairment of the sense of smell on either side. Visual acuity was 20/20 in each eye, but perimetric examination at this time

showed notching of the upper temporal field on the right and the upper nasal field on the left. The blind spots were enlarged in both eyes. The fundi showed the presence of papilledema, more pronounced on the left. There was definite weakness of the right side of the face, which was also evident on mimetic innervation. The tongue deviated somewhat to the right. There was slight motor weakness of the right side. The deep reflexes were more active, and the abdominal reflexes were diminished on the right. The right plantar response was equivocal. Temporal anomia was now present. Neither agraphia nor alexia could be demonstrated. It was observed that the convulsive episodes began with twitching of the right arm and that they were followed by weakness of the right side and by the appearance of a definite Babinski sign on the right. Uncinate phenomena or dreamy states had not occurred.

The clinical diagnosis of left temporosphenoidal neoplasm was made, and operation was advised.

Operation.—Exploratory craniotomy was carried out on Feb. 15, 1928. Under local anesthesia an osteoplastic flap was turned down on the left side, and the parietal and temporal lobes exposed. The dura was tense and did not pulsate. A needle was inserted into the posterior portion of the temporal lobe and about 10 cc. of dark brown semifluid material was evacuated. A second needle was introduced into the anterior portion of the temporal lobe with similar results.

The dura was incised; the brain appeared yellow and the convolutions flattened. The cortex in the temporal region was incised. A large necrotic mass was palpated in the depths, and about 15 cc. of the mass was removed.

The dura was left open. The bone flap was cut away slightly at its lower margin to allow a small decompression far from the motor cortex, and the flap was returned to position very loosely to permit an increase in intracranial volume.

Postoperative Course.—The patient has done fairly well since the operation. The convulsions have not returned. There have been no striking changes in the neural status except for the recession of the papilledema.

The location of the neoplasm, medially and deep, probably accounted for the thalamic pain on the right.

THE SURGICAL TREATMENT OF GLOSSOPHARYNGEAL NEURALGIA WITH REMARKS ON THE DISTRIBUTION OF THE GLOSSOPHARYNGEAL NERVE. By DR. BYRON STOOKEY.

This article appeared in full in the October issue of the ARCHIVES.

UNUSUAL INFECTIONS OF THE CENTRAL NERVOUS SYSTEM. By DR. JOSEPHINE B. NEAL.

In preparing this paper, two possibilities presented themselves. It would have been possible by a study of the literature to collect a large number of reports of unusual infections of the central nervous system. On the other hand, since 1910, when the Meningitis Division was established by Dr. Park, we have had an opportunity to study a large number of cases of acute conditions of the central nervous system and to determine the relative distribution of the infecting organism. It seemed that a presentation of these cases might be of more interest than that of cases collected from the literature.

From the summer of 1910 to January, 1928, we had seen in consultation 5,241 patients, most of them having some acute involvement of the central nervous system. In 1,942 cases a fairly definite diagnosis of some form of meningitis was made. The remaining cases, more than 3,000 in number, were made up of poliomyelitis, epidemic encephalitis, meningeal irritation with a variety of underlying causes, spontaneous meningeal hemorrhages and miscellaneous conditions. There were also a few cases of probable meningitis in which the diagnosis was not definitely made.

These 1,942 cases of meningitis were caused by the following organisms: the meningococcus in 708 instances; the tubercle bacillus in 855. It is to be noted that

during these years there has been no real epidemic of meningitis in New York City. In 1916, 1917, and especially in 1918, there was a rather sharp increase in the number of cases. Since 1920, the number of cases has fallen to low levels, until the rise this spring which is not recorded in these figures. Following the two most common infecting organisms, the meningococcus and the tubercle bacillus, comes the pneumococcus, with 145 cases. In ninety-eight instances the pneumococcus was typed: 30 were type 1; 17 type 2; 20 type 3, and 31 group 4. Streptococcus is fourth in the list with 123 cases. While not all the strains of *Streptococcus* were studied with sufficient care to make it absolutely certain whether or not they belonged to the hemolytic group, out of the relatively large number that have been so studied only one was found that did not hemolyze under suitable conditions. It is more or less well known that certain sugars, especially dextrose, interfere with hemolysis even with horse blood plates, and also that human blood, which is sometimes used in clinical laboratories for blood plates, hemolyzes less easily than horse blood. It is certainly our experience that, with rare exceptions, streptococcus meningitis is caused by a member of the hemolytic group.

The influenza bacillus is fifth in the list occurring in sixty-five cases. The staphylococcus is sixth with sixteen cases. Three of these were *Staphylococcus albus* and four *Staphylococcus aureus*. In the other instances the type was not determined. Next are the infections that are relatively unusual in our experience.

The colon-typhoid group: I (Neal, Josephine B.: Am. J. M. Sc. **172**:740, 1926) have seen only five cases caused by the *Bacillus coli* in pure culture. A sixth case was due to a mixed infection, one member of which belonged to the colon group. Two cases were due to Friedlander's bacillus, included by Park and Williams in the colon group. One case (Applebaum, E.: Arch. pediat. **42**:607, 1925) was caused by a *Bacillus paratyphosus* which developed during the course of meningococcus meningitis, but after the meningococcus had disappeared from the spinal fluid.

A study of the literature would indicate that the colon bacillus involves the meninges more often than our figures show. Frequently, however, the diagnosis was made at necropsy rather than during life; it seems probable, therefore, that in many instances the organisms may have been invaders just before or just after death and not the specific cause of the meningitis. Certainly our figures are in marked contrast to those of Barron (Barron, M.: Am. J. M. Sc. **156**:358 [Sept.] 1918) who reported, in 1918, forty-two cases—forty-one from the literature—of meningitis in the first three months of life. Of these, fourteen were caused by the *Bacillus coli* and only five by the meningococcus. In 1927, we (Neal, Josephine B. and Jackson, Henry W.: J. A. M. A. **88**:1299 [April 23] 1927) compiled statistics for children in the first three months of life and found that of fifty-three cases, twenty-five were caused by the meningococcus and only two by the colon group.

One of our two cases of Friedlander's bacillus meningitis was that of a child, aged 2½ years. Pneumonia and otitis media had also occurred, either of which might have been the primary focus of infection. The child eventually recovered. The second case was that of a man, aged 59, with otitis media. The case resulted fatally.

The condition in the five patients in whom *B. coli* was the inciting factor occurred at the ages of 2 weeks, 5 weeks, 8 months, 1½ years, and 6 years, respectively. In only two instances was a possible primary focus located, a pyelitis and an infected orbit from which the eye had been enucleated some months before on account of a retro-orbital abscess following measles. In the cases with pyelitis the infecting organism both in the urine and the spinal fluid was *Bacillus coli-communior*, which constituted a fairly definite relation between the two conditions. These five cases all resulted fatally, though one patient, aged 5 weeks, recovered from the meningitis but developed a hydrocephalus some three months later, from which he eventually died.

Micrococcus catarrhalis is relatively rare, only three of our cases being caused by it, at least so far as has been determined. It is of some importance, however, on

account of the ease with which it may be mistaken for the meningococcus unless a careful cultural study is made. An attempt to distinguish these organisms morphologically or by the appearance of the colonies is likely to result in errors, notwithstanding the statements to the contrary appearing in text books on bacteriology.

These cases were all in young children who were seen at the ages of 7 weeks, 8 months and 18 months, respectively. The child, 8 months of age, had a pneumonia which ran a rather rapid course, the patient dying on the fifth day of the illness. The case in the child, aged 18 months, ran a less acute course, twenty-two days. The infection followed measles and there was double otitis media. The most interesting case was that of the baby, in whom the diagnosis of meningitis was made at the seventh week, the illness having begun five weeks before with high fever, convulsions, vomiting and intestinal disturbance. When the patient was examined there was marked emaciation, opisthotonos and spreading of the sutures. Only a small amount of purulent fluid could be obtained by lumbar puncture. At the second visit, none of the fluid could be obtained from the spine, and ventricular punctures were necessary thereafter. Much of the time it was necessary to use a syringe to withdraw the fluid, even from the ventricle, and the fluid was often uniformly bloody. After it was found that we were dealing with *Micrococcus catarrhalis* instead of a meningococcus, an autogenous vaccine was given. The child showed some temporary improvement, whether from the relief of pressure or the vaccine I cannot say, and the quantity of fluid decreased. The improvement was temporary, however, and the baby died after being under treatment for a month, the total duration of the illness being more than two months.

There were two cases due to *Bacillus pyocyaneus*. Both resulted fatally. One case was that of a girl, aged 7, in whom the disease ran a rather subacute course, with typical signs of meningitis for about a month. There was no evidence of a primary infection. The second case, in a boy, aged 2, lasted for two months with two periods of marked improvement. Four doses of acriviolet in Ringer's solution were given the patient intraspinally without appreciable effect, either in the clinical condition or the growth of the organism. A culture of the pyocyaneus was isolated from the stool later in the disease. All the spinal fluids developed the characteristic greenish tinge on standing.

We have had two cases in which the genus *Proteus* (Neal, Josephine B., and Abramson, Harold: Am. J. M. Sc. **174**:665, 1927) was found in the spinal fluid, but in each instance another organism was present also. The first patient was a negro, aged 46, who was suffering from lobar pneumonia and definite signs of meningitis. He died at the end of five days. In the spinal fluid *Staphylococcus aureus* was found and also *Proteus mirabilis*.

The second patient, an infant, aged 5½ weeks, had a history of an illness of nine days' duration, marked by fever, restlessness, convulsions, vomiting and greenish stools. On lumbar puncture, only a few drops of purulent bloody fluid were obtained. On culture, the fluid yielded a gram-negative bacillus belonging to the genus *Proteus* and a gram-positive coccobacillus which would not be exactly classified but which resembled closely *Bacillus segmentosus*. It was necessary to resort to ventricular puncture to relieve the pressure, and the ventricles were injected with modified Ringer's solution. The quantity of fluid decreased and the gram-positive coccobacillus disappeared, but the *Proteus* persisted. The baby lived nine weeks after the meningitis developed.

Occasionally, a meningitis is caused by some organism that does not fall into any of the ordinary groups of pathogenic bacteria. Such a case occurred in a baby, aged 13½ months, who was seen within twenty-four hours after the onset of the illness, which had developed suddenly with fever, vomiting, convulsions and soon after marked apathy. On examination, typical signs of meningitis were found, including a few petechial spots on the body. The whole picture strongly suggested a meningococcic meningitis. On lumbar puncture, 30 cc. of cloudy fluid was withdrawn and 20 cc. of antimeningitis serum injected. The injections of serum were repeated twice. By this time it was certain that we were not dealing with a

meningococcus, and at the next two lumbar punctures no serum was given. The child made a rapid and uneventful recovery. The organism isolated was a gram-positive diphtheroid bacillus, quite pleomorphic, with some coccoid and comma forms. The organism was present in the smears of the first fluid, but no culture was obtained and it was at first thought to be a contamination. It was found in smears and cultures in the second and third fluids. The fourth and fifth fluids were sterile, and organisms were not found in the smears. The organism was nonpathogenic for mice, and a careful bacteriologic study was unsuccessful in placing it in any of the ordinary pathogenic groups.

We have had surprisingly few cases of mixed infections, only eleven. Four of the most unusual of these have already been referred to. A fifth, caused by the meningococcus and the staphylococcus was interesting in that the patient recovered with the usual treatment by antimeningitis serum. Most of the others were secondary to infections of the ear and were various combinations of the staphylococcus, streptococcus and pneumococcus.

The higher bacteria sometimes invade the central nervous system. We have had four cases due to the streptothrix. It is my impression that infections due to this organism are easily missed unless unusually careful bacteriologic work is done on the spinal fluid. On direct smears from the spinal fluids these organisms suggest either a more or less pleomorphic influenza bacillus, or a mixed infection of gram-negative bacilli and gram-positive coccobacilli. The characteristic branching forms do not appear until the organism has been cultivated for some days on suitable mediums. The strains which we have isolated have grown only anaerobically. Two of these patients were 11 months of age, one was 12 years and one 17 years. These cases were all of short duration—from five to eight days—and were characterized by extreme spasticity and greatly increased reflexes. The boy (Elmendorf, Ten Eyck, and Neal, Josephine B.: Arch. pediat. **42**:174, 1925), aged 12 years, suffered from a congenital heart lesion; the boy, aged 17, had an otitis media and one, aged 11 months, had bronchopneumonia.

The infections in man reported as being due to the streptothrix are comparatively rare. The lung is apparently the chief site of infection, but metastatic abscesses of the brain and the spinal cord are occasionally reported. In the few cases of meningitis in the literature, the disease was often secondary to an otitis media; however, this was present in only one of our few cases.

In all the infections that have just been described the spinal fluids have been distinctly cloudy or purulent, suggesting at once the presence of a meningitis due to one of the pyogenic organisms.

In the next two forms of infection, due to a pathogenic yeast, the torula, and to a sporotrichium, the spinal fluids were clear or slightly hazy.

We have seen two cases caused by the torula. One (Shapiro, Louis L., and Neal, Josephine B.: Arch. Neurol. & Psychiat. **13**:174 [Feb.] 1925) of these patients, 16 years of age, was under my observation for five months. In all, 133 lumbar punctures were done and a positive culture of the torula was obtained from the fluids in all except the last six. The second patient (Wortis, S. Bernard, and Wightman, Henry B.: Bull. New York Acad. Med. **4**:531 [April] 1928), a man, aged 21, at Bellevue, was seen by me only two or three times. He was acutely ill for only about three weeks, though for three and one-half months he had suffered from headache and increasing difficulty in vision. At one time there had been pus in the sphenoidal sinus. The torula was finally cultivated from the spinal fluid. Both these cases have been reported.

The case of (Hyslop, George H.; Neal, Josephine B.; Kraus, Walter M., and Hillman, Oliver: Am. J. M. Sc. **172**:726, 1926) sporotrichosis meningitis, in a girl, aged 15, was diagnosed by the presence of motile, refractile oval bodies in the hanging drop, by sporelike bodies, constantly present and by mycelial forms occasionally present in the direct smears. The disease in this instance was chronic, lasting nearly six months. This case has also been reported.

It is hardly necessary to emphasize the desirability of lumbar puncture in all cases presenting meningeal symptoms. It may not be amiss, however, to call

attention to the lack of meningeal symptoms in meningitis in infancy. While the onset is usually fairly acute, it is rarely so sudden as in later life. Practically always the disease is ushered in with a disturbance of the gastro-intestinal tract. The stools are usually loose and greenish or slimy. Vomiting is by no means as constant a symptom as it is in older children and adults. The gastro-intestinal symptoms do not respond to the ordinary methods of treatment. There is practically always an irregular fever. The child is usually irritable and hyperesthetic. There may be convulsions early, but they are by no means a constant feature, and they are not so severe as those that occur later in the disease. The classical signs of meningitis, such as rigidity of the neck and the Kernig sign, are usually entirely absent until the disease is well advanced. As a rule the reflexes at the beginning are normal. A bulging fontanel is practically always found. A hemorrhagic rash is rather unusual in infants. It cannot be too strongly urged that a lumbar puncture should be performed early in infants when the diagnosis is indefinite.

In conclusion, my experience with the methods used in examining spinal fluids in many hospitals and laboratories leads me to speak of the importance of a complete examination of all spinal fluids, and especially of the necessity for a thorough bacteriologic study. The examination of a stained smear is often misleading, as certain gram-positive organisms, especially the streptococcus and staphylococcus, decolorize readily in direct smear. I have already referred to the appearance of the streptothrix in smears. Cultures should be made from all fluids whether clear or cloudy, preferably from the centrifuged sediment, both aerobically and anaerobically on various mediums, and the cultures should be kept for at least two weeks before they are discarded as sterile. A careful examination of all spinal fluids with special attention to the bacteriology, would, I feel sure, result in the diagnosis of many unusual infections that are now missed.

DISCUSSION

DR. E. D. FRIEDMAN: There is not much to be said with regard to Dr. Neal's paper except to express our indebtedness to her for the mass of statistics which she has collected on the subject of meningitis, and for the excellent manner in which she has presented them.

I shall emphasize only one point made by Dr. Neal. She stressed the importance of recognizing the existence of meningitis in infants, in spite of the absence of the classical signs of this disease, namely, rigid neck and Kernig sign. Owing to the fact that the bones of the skull are not yet completely ossified and the sutures are still open, there is so much opportunity for distention of the subarachnoid space and the ventricles of the brain that little pressure is exerted on the spinal roots. This may explain the absence of classical signs of meningitis in early life.

DR. STOOKEY: Dr. Neal, our greatest authority on spinal meningitis, has presented in a concise manner a wealth of material and valuable deductions, and so scholarly a presentation it is rarely our privilege to hear. I should like to ask what she considers to be the most rational treatment for pneumococcic meningitis, which, I believe, with rare exceptions, has a mortality rate of nearly 100 per cent. Would opening the lumbar sac and basal cistern be of value by giving more permanent drainage?

DR. GEORGE HYSLOP: One point made by Dr. Neal I should like to emphasize —the necessity of repeated examinations of spinal fluids in patients who present a picture of diffuse meningitis and in whom the initial spinal fluid at least is unsatisfactory in providing bacteria that would be obvious on smear or on culture. I think that one of the torula cases which have been reported from New York in the last two years exemplifies this point. One of the other cases that Dr. Neal refers to, the case of sporotrichosis meningitis, also illustrated the necessity for repeated examination of spinal fluids that look clear.

DR. NEAL: All treatment of pneumococcus meningitis has been extremely unsatisfactory. All of my patients have died. I have very much better success

with streptococcic meningitis; I can recall three patients who have recovered, and it looks as if a fourth is likely to recover.

I have never had permanent drainage tried in any of my cases. Not all people have been equally unsuccessful in the treatment of pneumococcus meningitis. I recall, from the literature and personal reports made to me, that several patients have recovered. One case was reported in Brooklyn in which a combination ethylhydrocuprein hydrochloride and a suitable type serum were used, and I think two patients recently have recovered at Mount Sinai Hospital. I think that in both cases lumbar and cistern puncture were done, and I believe one patient received serum of a suitable type.

I do not know what is the best treatment. I have used serum of suitable type in a certain number of cases. In the last two or three years, however, since I have had what has seemed to be a rather more effective serum in the form of a concentrated preparation, the cases of pneumococcus meningitis I have seen have either been well advanced or else so rapidly fulminating that the patients have died before any treatment could have a fair trial.

In general, I think that drainage by lumbar puncture offers considerable relief in these cases. In studying the literature of the various forms of meningitis, more patients have recovered after lumbar punctures alone than with any one of the other means of therapy that had been tried.

If permanent, continuous drainage could be established it ought, theoretically, to be even more effective than repeated lumbar punctures, and I should certainly like to have it tried early in a series of cases to see what the result would be. In many instances where it has been tried in the past it has been instituted late, when the condition of the patient was practically hopeless, so that no means of treatment could be at all successful.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, May 25, 1928

N. W. Winkelman, M.D., *President, in the Chair*

The Presence of Air in the Subdural Space of the Posterior Fossa in Encephalography. Dr. W. J. Gardner.

I wish to present the encephalograms of three patients in whom some of the air injected by the lumbar route was found by the roentgen ray in the subdural space of the posterior fossa.

The first plate (fig. 1), in the anteroposterior view, shows well the winged effect produced by a subtentorial accumulation of air in the subdural space. These plates were taken with the patient in the erect posture. That this air cannot be in the subarachnoid space must be readily granted by all those familiar with the manner in which the arachnoid adheres closely to the sulci of the cerebellum. The second plate (fig. 2) shows the typical appearance of subtentorial air in the lateral aspect. Figures 3 and 4 illustrate further the appearance of air in this locality.

How does this air gain access to the subdural space if it is injected into the subarachnoid space? The answer to me seems apparent. The air collected beneath the tentorium in the subdural space has been, through an error in technic, introduced into the subdural space in the lumbar region. This may occur readily if there is difficulty in obtaining fluid during the injection of air, necessitating the frequent moving of the needle with consequent laceration of the arachnoid. Once the air is in the subdural space of the cord, there is little to prevent it from ascending to the posterior fossa where it becomes caught beneath the tentorium. Why it does not pass through the incisura of the tentorium is not yet apparent.

In the first two cases illustrated, there was considerable difficulty encountered in the withdrawal of the spinal fluid owing to some obstruction at the point of

the needle. In the third case illustrated, the withdrawal of fluid was carried out with ease, but near the conclusion of the operation a deliberate attempt was made to introduce air into the subdural space by withdrawing the needle until the fluid just ceased to flow. At this point 10 cc. of air was injected with the result shown in figure 3. The presence of air in this location does not give any unusual symptoms. Its rate of absorption has not been studied. Whether the subdural injection of air can be put to diagnostic use is not yet apparent.

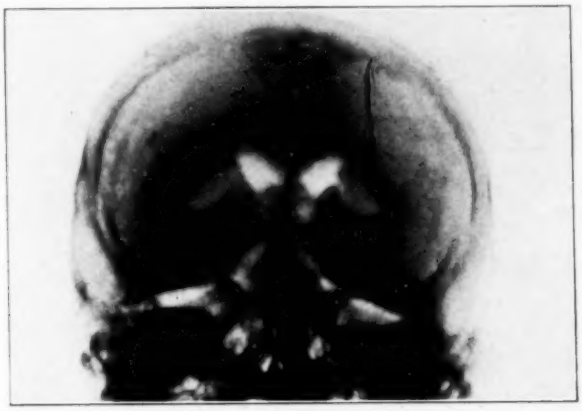

Fig. 1.—Anteroposterior view showing the winged effect produced by a subtentorial accumulation of air in the subdural space.

Fig. 2.—The typical appearance of subtentorial air in the lateral aspect.

DISCUSSION

DR. CHARLES H. FRAZIER: In the numerous opportunities that I have had to study the relation between the dura and the arachnoid, I have never seen any of the adhesions to which Dr. Fay refers and which he claims to be obstacles to the progress of air.

DR. LYNN H. HERSHEY: I observed a postmortem study which Dr. Gardner made, and when the dura was opened over the cisterna magna, a large free space was noted between the arachnoid and the dura. The arachnoid was intact.

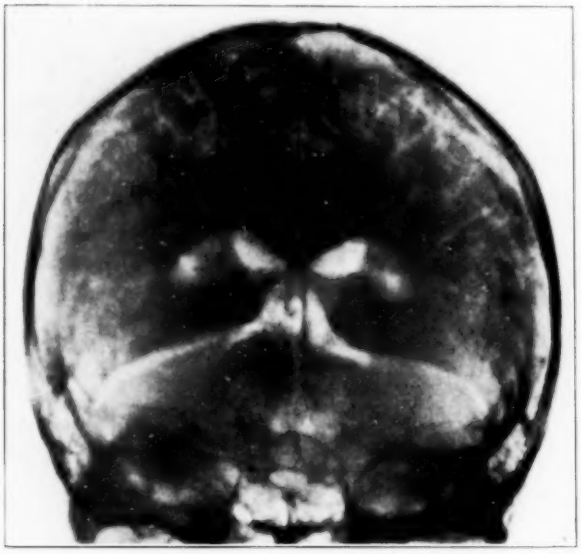

Fig. 3.—Showing further the appearance of subtentorial air in the lateral aspect.

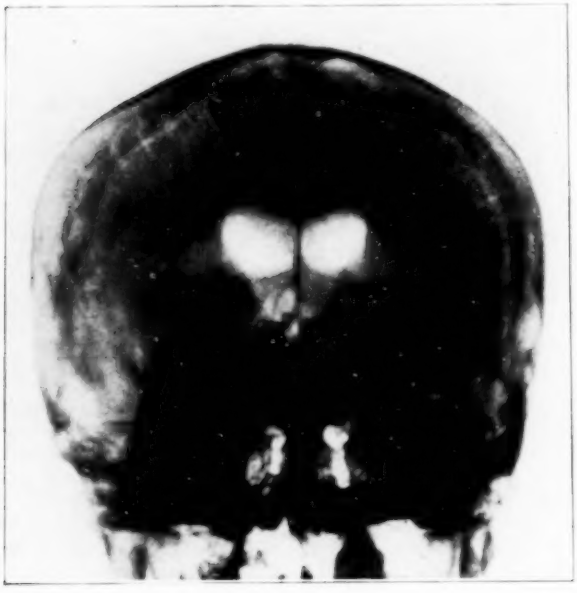

Fig. 4.—Showing further the appearance of subtentorial air in the lateral aspect.

This would tend to show that there is at least in some locations a free space between the arachnoid and the dura into which air could penetrate.

DR. RAYMOND W. WAGGONER: I have noted the air shadow described by Dr. Gardner in a number of cases in my series, and I agree with him in his explanation. This shadow seems to occur only when some difficulty has been experienced in getting the cerebrospinal fluid from, and the air into, the spinal canal. As there is a fairly large subdural space surrounding the cord, it is entirely possible that some of the air follows the course suggested by Dr. Gardner. I do not see how the mechanism described by Dr. Fay is compatible with the anatomy of the cerebrospinal system.

DR. GARDNER: In my experience I have not observed sufficient adhesions of the arachnoid to the under surface of the dura to preclude the passage of small bubbles of air.

TWO CASES OF COMPRESSION OF THE SPINAL CORD. DR. J. W. MCCONNELL and DR. HELENA E. RIGGS.

These two cases are presented as unusual cases of compression of the spinal cord, in which the conditions were materially improved by operation.

CASE 1.—J. O'N., aged 46, was admitted the the Philadelphia General Hospital in April, 1926, with the history of a sudden onset of sharp, lancinating pain in the left sciatic distribution one year prior to admission. This pain came on during sleep. It was intense and more or less continuous, so that the patient was forced to give up work. One month after the onset, a stretching operation was performed on the left sciatic nerve, without any relief from symptoms. Four days prior to admission to the hospital, there was a sudden onset of pain in the right sciatic nerve. The history was negative for any history of trauma to the spine or pelvis or for venereal infection.

On admission, the patient appeared ill and gave the impression of having lost a great deal of weight (40 pounds or 18.1 Kg.). His face had an anxious appearance and was haggard. He was able to walk only with the support of two canes, and he showed a markedly attenuated, limping gait, with a weakness of the muscles of dorsal flexion. Station was normal. The upper limbs and the cranial nerves were entirely normal. The abdominal reflexes were present and active. The lower limbs showed atrophy, especially marked in the muscles of the calf. Valleix's tender points were present over the course of both sciatic nerves, with the greatest tenderness over the sacrosciatic notches. Lasègue's sign was obtained bilaterally. Rotation of the lower extremity at the hip joint gave sharp pain referred to the hamstring and muscles of the calf. The patellar reflexes were present and active, but there was a bilateral loss of the achilles reflex. Abnormal reflexes were not obtained.

Examination of sensation in the lower extremities showed a loss of sense of position in both feet, and a loss of vibratory sense below the costal margin. Sense of touch was lost over the posterior portion of the left leg below the gluteal fold; on the right, it was impaired over the entire extremity. Pain and temperature sense showed marked impairment in both lower extremities, with the greatest impairment on the left. There was no involvement of the sphincter.

The Wassermann reactions of both the blood and the spinal fluid were negative. The spinal fluid was not under increased pressure; there was no evidence of spinal block. The spinal fluid, however, showed a trace of globulin. The x-ray picture of the spine and pelvis was normal. There was no clinical evidence of prostatic carcinoma.

Briefly, this patient showed a progressive spinal lesion, unconnected with any trauma. The onset was characterized by lancinating, paroxysmal, unilateral pain in the sciatic distribution which, during the progress of the condition, became bilateral. Examination, one year after the onset, showed atrophy of the muscle in the distal portions of both legs, with a loss of the achilles reflex. The sensory changes did not show any definite systemic involvement of the cord, and there

was no disturbance of sphincter control. On the basis of these observations, a diagnosis of neoplasm was made, probably intraspinal, involving, irregularly, the cauda equina and the lumbosacral fibers of the sciatic nerves.

Exploratory laminectomy was performed two weeks after admission. At the operation, a fibrous band, lying external to the dura, was encountered at the lower level of the fifth lumbar vertebra. This was about 0.5 cm. in width; it was definitely marginated and tightly encircled the entire cord. On removing as much of this as possible, the fibers of the cauda equina were seen to spread out.

Six hours after operation, the spontaneous pain was relieved, and superficial examination showed a beginning return of sensory function. The patient made an uneventful recovery, walking one month after operation and returning to work, as a stationary engineer, two months after admission to the hospital.

The microscopic study of the tissue removed at the operation showed dense fibrohyaline tissue with a few areas of calcification.

Case 2.—E. T., aged 59, admitted to the Philadelphia General Hospital in March, 1926, first noticed a sensation of numbness in the feet in 1924. This was worse at night and caused a certain degree of stiffness in walking. This condition progressed until eight months later when he was forced to walk with a cane; one year after the onset of the condition he was confined to a chair. Eighteen months after the onset, he first began to have pain in the legs. This was of a cramplike paroxysmal nature and became increasingly worse until admission to the hospital. One month prior to admission there was beginning weakness of sphincter control.

The patient stated that he had had venereal infection at the age of 30, for which he did not receive treatment until 1921. At that time, Wassermann tests of the blood and spinal fluid were 4 plus. For the next five years, he received intensive treatment. In 1916, he had a chronic cough, with loss of weight and night sweats. As a child, he had had scarlet fever and acute rheumatic fever.

Physical examination revealed a chronic fibroid tuberculosis of the upper lobe of the right lung and cardiac hypertrophy with a combined mitral stenosis and insufficiency. The spine showed a slight angulation at the eleventh dorsal vertebra and a marked bowing of the bones of the legs below the knees.

Neurologic examination did not reveal any lesion of the cranial nerves and the eyegrounds were normal. The upper extremities were normal except for an exaggeration of the reflexes. The upper abdominal reflexes were present and active; the lower were absent. There was relaxation of the lower portion of the recti muscles, giving the abdomen a "pot-bellied" appearance. The lower extremities were extremely spastic and presented a "lead pipe" type of rigidity. All reflexes were exaggerated to a marked degree, and ankle clonus was present. There was a Babinski sign bilaterally. All forms of sensation were diminished, almost to the point of total loss, below the level of the ninth dorsal vertebra, with a suggestion of a saddle-shaped area of preservation of sensation over the sacrum.

The spinal fluid was not under increased pressure; there was no actual spinal block, but after release of jugular compression, there was a slow return of pressure to normal. Wassermann tests of both the blood and the spinal fluid were negative, but there was a colloidal gold curve of 1111122100.

At this time a diagnosis of compression of the cord was made, but the causative factor was unknown. In the light of observations on the chest, the history and the angulation of the spine, the possibility of spinal caries was considered; with the history of a neglected syphilitic infection, gumma of the vertebra was a possibility. An x-ray picture of the spine at this time showed extensive rarefaction and sclerosis of the entire lower dorsal, lumbar and sacral vertebrae. The x-ray diagnosis was metastatic carcinoma, probably from the prostate, or, possibly, syphilitic involvement of the bone. Roentgenograms were then made of the entire skeleton, and the same proliferative and rarefying changes were encountered in the skull, clavicles, long bones and pelvis, as well as in the spine. The most marked changes were in the eleventh dorsal vertebra; here the bone

destruction was marked, and there was but little sclerosis. The diagnosis of osteitis deformans — Paget's disease — was made by Dr. Pancoast who also suggested the possibility of a second type of lesion in the eleventh dorsal vertebra — namely, bone sarcoma. Clinically, except for the bowing of the legs there was no evidence of Paget's disease.

Exploratory laminectomy was performed five weeks after admission. On exposing the lower dorsal vertebrae, the spinous processes were found to be so soft and spongy that they were removed by digital pressure. The dura was first exposed at the level of the eleventh dorsal vertebra. The cord appeared flattened and did not show pulsations. There was a decrease in the anteroposterior diameter of the spinal canal to the degree that a dural elevator could not be placed between the cord and the posterior wall of the vertebra. The spines of the ninth and tenth dorsal vertebrae were removed, and the cord slowly began to pulsate. The point of greatest compression was at the ninth dorsal; here the dorsal sulcus of the cord was entirely obliterated and splinters of bone penetrated the dura and were deeply imbedded in the substance of the cord. The histologic diagnosis of the bone removed confirmed the diagnosis of Paget's disease.

The patient's postoperative course was stormy owing to uncontrollable ooze from the bone. He left the operating table with a red blood cell count of 2,990,000 and 45 per cent hemoglobin. Trophic ulcers developed over the buttocks and sacrum, and there was an acute flare-up of the tuberculous process. Moreover, the patient developed an addiction to morphine.

Two months after operation the patient appeared to have less pain; he was able to move his legs and had fair control of his sphincters. There was little change in the neurologic observations, except for a fair return of touch and pain sensation in the previously anesthetic areas. Ten months after operation, sensation was normal throughout the lower extremities, but the patient was still under the influence of morphine, and the results were not considered trustworthy. At present there is no evidence of any sensory loss. The reflexes in the lower extremities are exaggerated but not spastic. The Babinski reflex still persists bilaterally. Motion is normal and there is no atrophy. There is a moderate degree of contracture of the left knee which is being corrected by tenotomies and physiotherapy. The abdominal muscles are of good tone, and there is an entire absence of the meteorism noted on admission. The lower abdominal reflexes are still absent. X-ray examination, one week previous to presentation showed that the osteitis deformans was still progressive. As yet there is no evidence of spinal block, as shown by a perfect conduction of the pilomotor reflexes. An interesting point in the recent examination is that the patient is apparently developing optic atrophy. This condition was mentioned by Paget in his original article and confirmed by others in advanced cases of osteitis deformans. In this case it is a question whether it is due to the disease of the bone, whether it is a late manifestation of neurosyphilis or whether it is merely an arteriosclerotic condition.

These cases seemed of interest because of the unusual causes of the compression (there is only one other report of a case of Paget's disease with compression of the cord on record) and because of the apparent improvement after operation.

THROMBOSIS OF THE ANTERIOR SPINAL ARTERY OF THE CORD. DR. LYNN N. HERSHEY.

History.—W. D., a man, aged 40, who had never previously been ill, while riding in an automobile, in September, 1926, was thrown upward so that the top of his head struck the top of the car. He was unconscious for sixty-two hours. He was also completely paralyzed in all four extremities and in bladder and bowel control. He complained of numbness and tingling of the body below the neck. There were no visual, auditory nor speech defects following return to consciousness. Beginning about five days after the accident, he began to use his arms and hands, and since then has steadily improved so that he can now walk, even without a cane,

and has fairly good power; however, he remains spastic. Three months after the accident he was severely burned on the left knee by a therapeutic lamp bulb, but did not suffer any pain.

Examination.—Weakness and spasticity were present in all four extremities. There was a "scissors" gait. All deep reflexes were exaggerated; there were bilateral Hoffmann's and Babinski signs, and ankle clonus. Atrophy and fibrillary twitchings were seen in the deltoids, infraspinatus and supraspinatus muscles of both sides. There was no disturbance of vibratory, position or deep pressure sensations. At the time of examination the patient recognized heat, cold and pain over the entire body, but there was a definite level of impairment which ended at the fourth cervical dermatome on the body and shoulders. There was a right sympathetic ocular palsy. The spinal fluid, two days after the accident, was crystal clear. Wassermann tests of the blood and spinal fluid were negative.

Diagnosis.—Since this man had symptoms of impairment of function of structures of the anterior half of the cervical cord, and also, according to what is probably the most recent work on the circulation of the cord, the 1924 edition of the textbook of Oppenheim, since the anterior half of the cord is supplied by the sulcal branches and the vasocoronal branches of the anterior spinal artery, I believe this man has a thrombosis, instead of a hemorrhage, of the anterior spinal artery in the fifth cervical cord segment, and possibly in a portion of the fourth. Against hemorrhage is the involvement of the anterior half of the cord only, the absence of the syringomyelic syndrome at the level of the lesion, and the crystal clear spinal fluid.

Comments.—Two similar cases, both with necropsy, have been reported in the literature. The first was by Dr. W. G. Spiller in May, 1909. This man had similar symptoms following the muscular exertion of lifting hundred-pound blocks of ice. At autopsy there was found thrombosis of the anterior spinal artery of the cervical cord, with sclerosis of the anterior half of the cord. The second case, was reported by Dr. Grinker and Dr. Guy (Grinker, R. R., and Guy, C. C.: J. A. M. A. **88**:1140 [April 9] 1927). The patient was a boy, aged 15, who suffered symptoms, similar to those of the patient presented, following the muscular exertion of stretching and yawning. After death which occurred a month later, there was revealed a thrombosis of the anterior spinal artery of the cervical cord, with softening of the entire half of the cord. Hemorrhages were not found, grossly or microscopically, in either case. In this case, I believe the blow on the top of the head, transmitted to the region of the neck, caused a temporary dislocation of one or more cervical vertebrae, with contusion of the anterior spinal artery, which was then followed by thrombosis. It is likely that some similar mechanism may be the cause of the injury and death sometimes seen from the rabbit punch of boxers and fighters.

In 1922, before the Philadelphia Neurological Society, Dr. Ornsteen presented the case of a girl who had taken some hot tea, and then immediately had gone out into severely cold weather. Soon she felt tingling and pain at the back of the neck, and on returning home was paralyzed in all four limbs. The residual symptoms were a spastic tetraplegia with atrophy of the muscles of the hand and forearm, diminished pain and temperature sensations of all four limbs and trunk, and diminished vibratory and position sensations in the toes. The symptoms of the posterior column were explained by an extensive thrombotic lesion reaching from the eighth cervical region to the median fillet decussation in the medulla.

In 1925, Dr. Alpers presented a case of thrombosis of the anterior spinal artery of the lumbar region of the cord. His patient showed paralysis, fibrillary twitchings and atrophy of the muscles of the leg.

DISCUSSION

DR. W. B. CADWALADER: Dr. Hershey's case is most important because trauma as a cause of thrombosis of the anterior spinal artery is so little known. When the anterior spinal artery becomes occluded, without trauma, the condition is

generally syphilitic. Experiences of the World War proved that the impact of a bullet against the spinal vertebrae alone, without fracture, was capable of producing softening of the substance of the spinal cord without hemorrhage. It seems not impossible that in such cases thrombosis of the anterior spinal artery might have produced transitory vertebral luxation, thus being responsible for the myelomalacia. In Dr. Hershey's case, the character of the trauma, I think, is important in explaining the character of the lesion.

DR. CHARLES K. MILLS: I wish to congratulate Dr. Hershey who has presented his case in such an admirable manner. He clearly brought before our minds the condition of occlusion of the anterior spinal arteries. It is interesting to know how the occlusion came about. Apparently it was due to strong compression of the head, such as might result from a severe blow or fall.

RESIDUAL SYMPTOMS PRESENT IN A PATIENT ONE YEAR FOLLOWING REMOVAL OF AN ENDOTHELIOMA IN THE LEFT CEREBELLOPONTILE ANGLE. DR. TEMPLE FAY.

T. H., aged 17, presented at the time he was referred to me by Dr. V. K. Hart, of Statesville, N. C., choked disk, headache, vomiting, failing vision and deafness in the left ear. Marked ataxia on the left, with pyramidal tract symptoms on the right were also present. The patient was operated on under local anesthesia, and the left cerebellopontile angle was exposed by means of a new operative approach, using the midline incision and carrying a cross cut to the mastoid on the left. A hemisuboccipital craniectomy was done; the ventricle was tapped and ample exposure was provided by the unilateral approach. A tumor was seen in the angle about the size of a walnut. It was partially cystic, and was removed in its entirety, except for the attachment of the base of the cyst, well into the angle. The patient had a stormy convalescence for a period of three months and a slow recovery. He shows the following symptoms at the present time: almost complete return of hearing on the left; vision normal, with correction; fields full; no headache, vomiting or choking of the disks; slight ataxia in the finger-to-nose test and in the use of the left leg; slight staggering to the left on walking. In all other respects he is normal.

He was presented from the standpoint of a hemisuboccipital craniectomy, as a desirable means of approaching the cerebellopontile angle, and from the excellent postoperative recovery which he presents at the end of one year.

A CASE OF ATYPICAL NEURALGIA. DR. TEMPLE FAY.

R. K., aged 65, was presented complaining of pain, deep in the eye, in the malar region, back of the ear and down the neck.

In five successive operations the following structures have been sectioned to relieve the pain: (1) avulsion of the sphenopalatine ganglion, under the direct method, trans-zygomatic; (2) section of the entire posterior root of the trigeminus, on the left, with resultant anesthesia; (3) section of the gray rami, as well as the superior cervical sympathetic (Hunter-Royle operation); (4) stripping of the carotid artery on the left. The previous operations failed to relieve the pain, although the carotid sympathectomy apparently helped; pain returned in the same distribution. As the only sensory structures remaining which apparently could give rise to a complete pathway to the brain, the ninth and vagus nerves were considered. Section of the sensory branches of the vagus, including the jugular branch and the sympathetic, as well as of the glossopharyngeus, has been accompanied by complete relief from pain so far.

It is questionable whether sufficient time has elapsed to permit the drawing of any conclusions. The patient states that the last operation was the one which has relieved him most. Three other cases of section of the sensory branches of the vagus have been associated with complete relief from pain. The results of this method will be published in full when sufficient time has elapsed to warrant any conclusions.

DISCUSSION

DR. MILLS: It does not seem to me that Dr. Fay has clearly shut out involvement of the glossopharyngeal nerve, although he has seemed to have shown destruction of the fifth, seventh and eighth to some extent; also, I understand, he did remove the pneumogastric. I think he must have cut the roots of the glossopharyngeal in his operation. The case seems to me much like the one of glossopharyngeal tic doulourеux which has so well been described by Dandy.

DR. BERNARD J. ALPERS: It looked from where I am sitting as if the patient had atrophy of the face; I would like to know what Dr. Fay thinks about this. I think it might possibly throw some light on the question of progressive facial hemiatrophy.

FRACTURE OF THE SKULL WITH FOCAL EPILEPSY AND PARALYSIS SUCCESSFULLY TREATED BY OPERATION. DR. J. H. LLOYD and DR. CALVIN M. SMYTH.

A young man was admitted to the Methodist Hospital with a history of having been thrown from a second study window while intoxicated. He was conscious on admission but somewhat intoxicated. The external evidences of injury were: (1) laceration of the scalp in the occipital region; (2) contusion of the right leg; (3) bleeding from the right ear (drum head intact); (4) fracture of the pelvis; (5) fracture of the acromion process of the left scapula.

The fractures were confirmed by the x-ray examination, which also showed a linear fracture in the right temporoparietal region and another fracture through the right mastoid. Neither fracture showed depression.

Neurologic examination at this time did not show evidence of any intracranial lesion.

On the third day following the accident, the pulse rate dropped to 58, the patient began to complain of headache and the blood pressure was 110 systolic and 55 diastolic. He was given 40 cc. of 50 per cent dextrose intravenously and a spinal puncture was done; it showed bloody fluid under increased tension. Temporary improvement followed.

Spinal puncture was repeated on the fourth and fifth days; the fluid remained under tension but did not contain blood. On the tenth day, the patient became sluggish and an overenthusiastic resident withdrew 30 cc. of spinal fluid without the use of a manometer. On the following day the patient became comatose and developed a left-sided hemiplegia. Dr. Lloyd saw him in consultation and advised a decompression operation. This was done on the right side in the subtemporal region, eleven days after the injury, under local anesthesia. A subdural clot was removed. This was followed by slight improvement in the general condition for twenty-four hours. The patient then began to have typical jacksonian seizures, involving the left arm and face. He had fifty-six of these in twenty-four hours. Dr. Lloyd saw him again and advised wide exposure of the right precentral cortex if the general condition permitted.

Fifteen days after the injury, an osteoplastic flap was turned down. A bleeding vessel beneath the dura was located and secured by transfixion ligature. Pulpified brain was seen in the upper part of the precentral convolution. Following this operation the convulsions ceased, and the patient has had none since. Motion returned in the left arm on the third day and in the leg on the fifth day following the second operation.

The patient finally made a good recovery and was discharged on the seventy-first day following the accident. On discharge the spinal fluid was under normal pressure; the eyegrounds and visual fields were normal; the flap was firmly united to the skull. The patient has complained of occasional headache but nothing more. He is not working, but is going about and says that he feels well.

DISCUSSION

DR. J. HENDRIE LLOYD: I have said that focal epilepsy in fracture of the skull seemed to be comparatively rare. A recent paper by Reichmann, based on

the reports of 613 cases of fracture of the skull, shows that in only twenty-three cases, or only 4 per cent, did epilepsy occur; and that in only one half of these, or less than 2 in 100 cases of fracture, the fits were jacksonian in type. In Dr. Smyth's case, the fits did not begin until the twelfth day. They were purely focal, confined to the left arm and face, and were frequent — fifty-six in twenty-four hours. During the time I was examining and watching the patient, less than one hour, he had three of these seizures which were violent; he was in status epilepticus. He had the last fit just as he was being carried to the operating table This prompt result from operation is most interesting. The hemiplegia cleared up rapidly, and has left only a slight hemiparesis. The prognosis in such cases may remain a little doubtful for a while, and the patients ought to be observed after they leave the hospital, even for a year or more. There has been no return of the seizures since the operation, more than four months ago.

The operation of choice is the osteoplastic flap. An ordinary trephine opening is not enough to allow the surgeon to explore the brain. In this case the first operation by the trephining was not effective; in fact, the epilepsy and hemiplegia did not occur until after the first operation. The osteoplastic flap gave complete relief. In every case of fracture of the skull, even though there is entire absence of nervous symptoms, a lumbar puncture should be done and if blood is found in the spinal fluid, it should be regarded as an indication for an exploratory operation. Fracture of the skull is becoming common, largely from automobile accidents, and these cases demand the careful consideration of the neurologist as well as of the surgeon. Because of the grave complications in Dr. Smyth's case, the good results obtained are noteworthy.

Dr. Smyth: Answering Dr. Fay's question as to how the shock was treated in this case, the patient received the usual things in the way of stimulation: fluids by vein, under the skin, etc. As to the possibility that dehydration and dextrose might have accomplished the same result as an operation, I neglected to state that this man received intravenous injections of 50 per cent dextrose and magnesium sulphate by bowel with only temporary improvement, and it was not until after the second operation that the symptoms began to abate. Following the operation he continued to receive dextrose by vein with satisfactory results. The hemorrhage disclosed at operation was subdural but extra-arachnoid.

Major Hysteria with Attacks of Impaired Circulation in the Left Upper Limb. Dr. William G. Spiller.

The case reported was one in which severe convulsive attacks with opisthotonus occurred in a young man after a violent blow on the head in the occipital region. The condition was that usually recognized as major hysteria. The man also had attacks in which the left upper limb showed marked vascular discoloration and alteration of the pulse. These vascular attacks were frequently, but not invariably, associated with the convulsions.

The severe blow on the head followed by these symptoms gave occasion for a consideration of the latter as a result of a substriate or subthalamic hemorrhage, and of the relation of certain hysterical conditions to organic changes, such as are seen in epidemic encephalitis. Reference was made to the ability of a few persons (the cases of whom are reported in the literature) to control the pulse of the upper limb by pressure on the axillary artery resulting from the position of the limb, and it was considered as probable that a similar condition existed in the patient reported in this paper. The paper will be published in full in the *Journal of Neurology and Psychopathology.*

DISCUSSION

Dr. Cadwalader: Dr. Spiller's presentation is an exceedingly important one because it opens a new field of thought in explaining certain hysterical manifestations on a logical physiologic basis.

A state of swelling and bluish discolorations of the paralyzed limb in hysterical patients was recognized many years ago, especially by the French, and has been called "blue edema." Probably this was similar to the cyanosis that Dr. Spiller has described in his patient. During the war in France similar cases were often observed. I have seen an hysterical patient in whom one hand was held so tightly clenched that it was impossible for the examiner to open it, even with considerable force. The hand had become extremely cyanotic.

Gustave Roussy of Paris described his experiences before the meeting of the American Neurological Association in 1920, with a variety of different types of hysterical contractures seen during the war in France, and explained how prolonged fixation of the joint due to hysterical muscular contracture is capable of producing local effects secondarily in the affected limbs, manifested by different degrees of circulatory and trophic disturbances in the tissues, including cyanosis.

Dr. A. M. Ornsteen: Dr. Spiller's discussion of the association of functional symptoms with organic states and vice versa suggests the strong possibility of functional symptoms having an organic basis. But to me this does not necessarily indicate an all-inclusive theory. By that I mean to imply that psychogenic mechanisms may release certain definite symptoms and signs through pathways utilized by mechanisms of an organic nature thus causing the expression of the two disorders to be identical. Therefore one sees so-called functional signs in both organic and functional disorders. Nevertheless, it should make one hesitate to call some conditions absolutely functional when there is a possibility of an undiscoverable organic basis.

Dr. Spiller referred to a patient reported by Dr. Sokalansky who had peculiar psychic spells occurring during epidemic encephalitis, which further illustrates the practically inseparable association of psychic mechanisms and physiologic somatic functions, as in the disappearance of the man's almost utter helplessness during one of these attacks.

Referring again to the association of organic and functional psychic reactions, I wish to refer briefly to a patient who has an advanced form of paralysis agitans of the encephalitic variety who, for the past three weeks, has been having a number of attacks a day of the following nature: She experiences a soreness over the precordium which then radiates into the epigastrium, as a result of which she becomes anxious, restless and begins to cry. She soon experiences a cold feeling throughout the body, as though a frost were passing over her lips. Then the extremities and lips become cyanosed, the left hand from the finger tips to the knuckles becoming greatly darkened. She then suddenly calls out that she is dying and wishes to be put in a sitting position; when this is done she experiences a sensation as though everything in her body suddenly dropped. During the attack she lacrymates freely, particularly in the left eye. I wish to call attention to the fact that the cyanosis of the left hand is much more marked than that of the right, and the lacrymation is more marked in the left eye. In this connection, it is interesting to note that the parkinsonian syndrome is more advanced on the left side. These associations to me are significant. I believe that the release of these phenomena is due to an organic condition of the mesencephalic sympathetic nerve centers and is probably more marked on the right side of the brain, as shown by the occurrence of the stronger symptoms and signs on the left side of the body where the motor rigidity is more marked.

I believe also that psychogenic factors may operate through subcortical pathways and initiate symptoms of this character in various psychic states. In this connection, one may recall the frequent observation of acrocyanosis in young patients with dementia praecox.

Dr. F. N. Anderson: I saw one of the early attacks before the convulsions occurred in which the cyanosis was definitely marked. It was at a level 3 or 4 inches (7.62 or 10.16 cm.) above the elbow, and disappeared before I could start to make notes about it. My other observations were made at the time of the convulsions.

A Case of Pseudosclerosis. Dr. Charles S. Potts and Dr. Winifred B. Stewart.

History.—M. K., was admitted to the neurologic ward of the Philadelphia Hospital on April 24, 1915, complaining of generalized tremor. She stated that she had been perfectly well until six months before admission, when she was badly frightened by an intoxicated man. Shortly after this she was seized by attacks of trembling, which involved the entire body. These attacks increased in frequency and duration until, at the time of admission, the tremor was almost constant. She did not complain of any other physical disability. She had had the usual diseases of childhood, and, aside from the fact that her father was a habitual drunkard, the family history was unimportant. She was a cigar worker by trade.

Physical Examination.—The patient was a well developed and nourished white woman, aged 20, with a mentality slightly below normal, showing no evidence of visceral disease. There was no tremor when she was at rest, but on the slightest mental or physical effort she showed coarse clonic tremors of the head, trunk, arms and legs. This tremor was proximal rather than distal, involving the elbows and knees rather than the fingers and toes. There was little, if any, muscular rigidity. The reflexes were not exaggerated, and the abdominal reflexes were present. There was no Babinski sign or clonus. When walking there was a tendency to lean forward, and there were backward and forward motions of the head and, at times, of the trunk, with a coarse tremor of one arm and then of the other, and sometimes of both. She showed no ataxia; the cranial nerves were normal, and there were no abnormalities in sensation.

Since she has been in the hospital she has become progressively worse. The tremor in the legs has become so violent that she is unable to walk, although there has been no loss of actual muscular strength. Her speech has become hesitant and more or less explosive, but there is no evidence of scanning, and it is not monotonous. Indeed, the difficulty seems to be with breath control rather than with articulation. She has slowly deteriorated mentally, showing great emotional instability. There is, however, no definite evidence of a psychosis.

She has had no illnesses since admission to the hospital. There have been no symptoms suggestive of disease of the liver. In 1920, she had had an uneventful pregnancy and was delivered of a normal child.

The blood chemistry has always been normal. The serology of the blood and spinal fluid is normal, and the colloidal gold curve is normal.

At present she shows little, if any, tremor when at rest, but on physical or mental effort the tremor is violent and of the type described. The muscular strength is good, and there is no rigidity. The reflexes are present but not exaggerated. There is no enlargement of the spleen or demonstrable abnormalities of the liver. Examination of the eyes on several occasions has shown neither nystagmus nor abnormalities in the extra-ocular movements, and no pathologic process in the nerve head. Dr. Holloway, on recent examination, demonstrated the presence of a Kayser-Fleischer ring at the corneal-scleral junction in both eyes. This ring is not complete, but is present only at the upper and lower quadrants of each cornea.

Diagnosis.—The fact that this patient does not give any evidence of involvement of the pyramidal tracts, has active abdominal reflexes and has neither nystagmus nor changes in the eyegrounds, excludes the diagnosis of multiple sclerosis. On the other hand, the character of the tremor, with the absence of these symptoms, the age of onset, the mental deterioration, and the presence of a Kayser-Fleischer ring lead to the diagnosis of lenticular degeneration of the pseudosclerosis type.

DISCUSSION

Dr. Charles S. Potts: We had intended showing another patient, one of a family of three brothers and one sister, who present symptoms like those of this patient. Dr. Cadwalader showed one of the family in 1913. He might be interested in knowing that they are all living and well.

The duration of the disease in this patient is also unusual, as the symptoms first appeared in 1914 or 1915. She was admitted in 1915. We have called it pseudosclerosis, but recognize that that is not a good name. It is the tendency now to consider pseudosclerosis and Wilson's disease as the same disease. The symptoms of this patient are not what I consider those of Wilson's disease. The Kayser-Fleischer line is interesting because it is usually supposed to appear early and to have some connection with the condition of the liver. As is known, the liver may be diseased and not give rise to any symptoms. Barnes and Hurst, in a recent paper on lenticular degeneration, said that every patient with a Kayser-Fleischer line that came to autopsy had disease of the liver. According to Hall, this line was present in all of sixteen cases in which the condition was diagnosed as pseudosclerosis; of twelve cases diagnosed as Wilson's disease it was present in only 50 per cent.

In reference to the view that this might be hysteria, when the patient first came into the hospital the condition was so diagnosed. I consider hysteria a rather dangerous diagnosis to make, and I believe that there are more cases called hysteria which turn out to be something else later than vice versa. This patient has had gradual progression of symptoms since entering the hospital and has had none of the stigmas of that disease. I am certainly not convinced that this is hysteria. The Kayser-Fleischer ring does not occur in hysteria but does in certain forms of lenticular disease.

In reference to the family reported by Dr. Cadwalader, there are four members with symptoms somewhat like those of this patient, and Dr. Cadwalader said that when he showed his patient here, a diagnosis of hysteria was made by some. I have seen his patient lately and it certainly is not hysteria now.

I believe that our case comes under the classification of pseudosclerosis. Pseudosclerosis, Wilson's disease and dystonia musculorum deformans all have been put into the class of progressive lenticular degeneration by some, and thought to be modifications of the same thing. I am inclined to this view. When other parts of the brain are involved, as is often the case, symptoms may vary, according to the different locations of the lesions. About a year ago, Barnes and Hurst reported a case in which the lesions were most marked in the frontal lobes. Seletzky in Germany has published a paper in which he claims that all cases of so-called pseudosclerosis are either multiple sclerosis or Wilson's disease and that Wilson's disease is a form of encephalitis.

DR. LLOYD: I hesitate to form an opinion in this case on such short notice. It seemed rather enigmatic. I think the diagnosis of hysteria should be carefully taken into account. The mode of onset, following an emotional shock, and the character of the movement itself, which is not so much a tremor as a choreiform movement, suggest this diagnosis. I have seen some cases of severe hysterical tremor which were just like this and in which the patients recovered.

DR. MILLS: I agree with Dr. Lloyd that the case of Dr. Potts is to me very much like one of hysteria. I have seen more than one such case of hysteria. The intention tremor, ataxia and irregular breathing may all be explained by the diagnosis of hysteria. In many cases of so-called pseudosclerosis there is something indefinite about the reports.

DR. CADWALADER: Dr. Potts has said that his case of familial tremor was probably a case of pseudosclerosis and has compared his patient to one I presented here in 1913 as a case of progressive lenticular degeneration. Severe tremor and the resulting incoordination are the most striking features of Dr. Potts' case. The extreme muscular rigidity and contractures which my patient had and which are usually noted in advanced cases of Wilson's disease seem to be lacking. It is interesting to know, as Dr. Potts and Dr. Stewart have pointed out, that, in this familial form of disease, different members of the family may be affected differently, one presenting generalized tremor as in Dr. Potts' patient, and the brother, a high degree of muscular rigidity with contractures. By some, especially in Germany, the pseudosclerosis of Westphal and Strümpell is thought to be intimately related to the progressive lenticular degeneration of Wilson.

TWO CASES OF TUMOR OF THE BRAIN WITH FEW LOCALIZING SYMPTOMS. DR. RAYMOND W. WAGGONER.

Great difficulty is often experienced in the localization of tumors of the brain in certain so-called silent areas. In other regions, tumors almost invariably present definite signs and symptoms of localizing value in addition to the general symptoms of intracranial tumors. I wish to record the cases of two patients from the service of Dr. Charles H. Frazier, at the University Hospital, in whom tumors were found in areas not usually regarded as silent; yet these patients had few localizing symptoms and, in one, the symptoms present were definitely misleading.

CASE 1.—R. R., aged 24, entered the University Hospital with the complaints chiefly of difficulty in reading, headache and paresthesia of the right leg. The first symptom noted was numbness of the right leg; this had been present for two and a half years. It was not constant, but came on in attacks. The area involved gradually increased until the whole left side of the body would be numb. At this time there was noted some difficulty in speech, probably a dysarthria. The severity and scope of these attacks then gradually diminished until, just before admission, only the leg was involved. Two and a half months before admission he began to have some loss of visual acuity so that he experienced great difficulty in reading. This was followed by transient attacks of blindness which lasted from two to five minutes. These attacks may involve one or both eyes and occur at irregular intervals. Recently, there has been a more or less constant, bilateral, dull aching pain in the occipital region. The past medical and the family history were essentially unimportant. The patient was married, but has been separated from his wife for some time. He has taken alcohol to excess, but has used none during the past nine months.

The physical examination gave entirely negative results. There were no positive neurologic symptoms. Symptoms of the parietal and temporal lobes were conspicuous by their absence.

The cerebrospinal fluid pressure was 40 mm. of mercury, and there was a field count of 7 red blood cells and 4 white cells. Serologic tests were negative. Examination of the urine showed the presence of a faint trace of albumin on three occasions.

X-ray plates of the skull were reported as normal.

Examination of the eyes showed a visual acuity of 6/12 in the right eye, 6/60 in the left eye and a contraction of the color fields with an enlarged blind spot. There was a slight horizontal nystagmus on lateral deviation of the eyes. The retinal arteries were contracted. A few fresh hemorrhages were present with a bilateral choked disk of 7 diopters.

Operation.—It was decided to do a ventricular estimation, but when the cannula was introduced toward the left ventricle, a solid mass was encountered. This was supposed to be the tumor, and an osteoplastic flap was made over this area in the parieto-occipital region, exposing a large fibroblastoma which was removed.

Course.—The patient made a good postoperative recovery, but examination before discharge showed evidence of a slight right hemiparesis and a slight aphasia. The patient's convalescence was good, and three months after operation he was almost free from symptoms, although there were still paresthesia of the right side and secondary atrophy of both optic nerves.

CASE 2.—This patient, very much like the first, a man, aged 43, married, entered the University Hospital on Dr. Spiller's service complaining of attacks of mental confusion and of severe headache. Six years before admission to the hospital he had had a nervous breakdown characterized by a dazed mental state, exhaustion, loss of weight and a condition of the skin diagnosed as "shingles." After a six month's vacation he was much improved, but a similar condition again developed two years later. Two years before examination he was in an automobile accident, which resulted in a slight injury to the left side of the head. In June, 1927, he

had an attack during which he was disoriented and "silly." This attack lasted two or three hours; then he became unconscious and had a convulsion. He was taken to a hospital where he remained for five days without further convulsive seizures. Shortly after this the patient complained of lack of energy, and seemed dazed and confused — so much so that he had to discontinue work. The last attack began three weeks before admission. At this time he was extremely weak and after seven days was confined to bed. At the same time he complained of severe occipital headaches which he described as "drawing and lightning-like." He would have as many as two attacks of headache a day, each lasting about one hour. He had also a constant, dull aching headache. During this period of two weeks he had some projectile vomiting, and vision had been blurred. At times, he would misplace syllables of words when talking. He had difficulty in concentrating and had some difficulty in understanding what he read, although there was no word deafness. He had never been a vigorous man, and was always of the nervous, worrying type. He had had an appendectomy performed in 1906, and it was complicated by pneumonia.

Physical Examination.—Examination revealed a bony elevation of the skull in the left parietal region, large and injected tonsils and a distended abdomen. The respiratory rate was slow. The patient was in a semistuporous condition, but could be roused and would reply to a question. The achilles and patellar reflexes were a little exaggerated but equal on the two sides. There were positive Hoffmann and Babinski signs on the left, slight weakness of the left upper limb, but no weakness of the left lower limb. There seemed to be a slight incoordination in the use of the left side. At the same time there seemed to be a slight weakness of the right side of the face.

Examination of the eye gave almost entirely negative results, there being only a slight bilateral right upper quadrantic cut. There was no choking of the disks.

The urine consistently showed the presence of a trace of albumin.

X-ray pictures showed an irregular rarefied area in the left parietal bone with a tendency to perpendicular striation in this region. There seemed to be some inward thickening of the bone. The appearance was not unlike an osteomyelitis of syphilitic origin. There was almost complete atrophy of the dorsum sellae which was taken as an indication of increased intracranial pressure.

Operation.—An osteoplastic flap was turned down, which included all of the bone which was known to be involved as shown by the x-ray. The diseased bone and a large fibroblastoma were removed. The patient is now practically free from symptoms.

Comment.—This case is particularly interesting because of the ipsilateral symptoms. The positive Hoffmann and Babinski signs were both on the left side. The motor incoordination and weakness were on the left side, and yet the tumor was on the left. In this instance, the appearance of the skull bone as shown by the x-ray played a large part in the localization of the lesion. The apparent thickening and rarefaction of the bone immediately over a fibroblastoma have been noted before. These observations by the x-ray seem to be almost pathognomonic of a fibroblastoma.

DISCUSSION

DR. FRAZIER: I think the reports speak for themselves. I was especially interested in the first case because up to within a short time before the operation the diagnosis of epilepsy had been made. The patient had exhibited attacks at various intervals with numbness on one side of the body, and it was not until a short time before the operation that he developed signs of increased intracranial pressure, of a degree much higher than one usually observes in pretentorial growths.

With regard to the second case, I wish especially to call attention to the unilateral headache — this is not uncommon with endotheliomas. I regard it as an important sign in localization and differential diagnosis.

EXHIBITION OF SPECIMEN OF TUMOR OF THE FRONTAL LOBE OF HUGE DIMENSIONS IN A CHILD, WITH TRIFLING PHYSICAL DISCOMFORTS AND DISABILITIES. DR. CHARLES H. FRAZIER.

This specimen is presented because: (1) the tumor is the largest encapsulated growth; (2) the tumor was an endothelioma, infrequent in children; (3) a tumor of this character had attained such enormous proportion in so short a time; (4) there was change in the skull shown by the x-ray; (5) there was no evidence of a profound increase in pressure, and (6) there was a reasonable degree of uncertainty as to laterality or localization.

The patient was a child, aged 3, with a history of a normal delivery with instruments, and no abnormalities at birth. She was perfectly well with the exception of the diseases of childhood. When the patient was 2 years of age, a year before admission to the University Hospital, the mother noticed that the child stumbled when playing with other children, and that there was a certain amount of clumsiness which seemed limited to the right side. The head seemed to be increasing in size more rapidly than it should. The child's appetite seemed abnormally large. In December, 1927, three months before admission to the hospital, she began to complain of headaches and seemed restless. In January, 1928, there was an attack in which the child did not fall or lose consciousness; it was characterized at first by pallor then by cyanosis of the face and rigidity of the body. There was a second attack of similar nature a few days later, and after this the mother noticed more clumsiness and apparent weakness of the right arm and leg.

Physical Examination.—Physical examination revealed nothing of moment except the size of the head which seemed in the biparietal diameter to have greater prominence on the left side.

Neurologic examination revealed that in running or walking the child seemed to swing the right foot and to hold the right upper arm rather close to the side.

Because of the age of the patient, it was extremely difficult to apply the ordinary tests for dysfunction, but it appeared as though there was inaccuracy in the right finger-to-nose test, and none in the left; there was also a suggestion of weakness in the distribution of the left facial nerve. The station with feet together was unsteady although she would not close her eyes.

Under the effect of dehydration the child did not seem to complain of so much headache. There was less evidence of weakness on the right side.

In his examination, a day or two later, Dr. Spiller was of the opinion that there was some loss of innervation of the left angle of the mouth; that all movements were incoordinate; that the child seemed to use her left hand in preference to the right and that the right patellar reflex seemed exaggerated.

Ophthalmic examination revealed that the retinal vessels appeared somewhat tortuous, the disk margins somewhat veiled and their color gray. Vascularity was fair, and there was 1 diopter of choking and a suggestion of postpapillitic atrophy.

Laboratory Examinations.—X-ray examination revealed the skull to be thin, with widening of the sutures and enlargement of the pituitary fossa. Results of examination of the blood and urine were normal. Examination of the cerebrospinal fluid gave a protein content within normal limits.

Ventricular estimation revealed an enlarged left ventricle and a collapsed right ventricle; the ventricular diagnosis was: supratentorial tumor on the right.

Withdrawal of 155 cc. of fluid from the left ventricle with injection of 5 cc. of air was performed. From the right ventricle only a few cubic centimeters of fluid escaped, and 5 cc. of air was injected. The interpretation of the x-ray films was: hemispheric tumor, right frontal.

Craniotomy.—A flap from the right frontoparietal region was reflected. Subdural tension was extreme. The dura over the frontal lobe was adherent to the cortex, and a firm tumor was felt on palpation. It was decided not to attempt removal of the tumor at this sitting, and the flap was closed.

Termination.—The child died within twenty-four hours of the operation, possibly from operative shock, although the operation was limited in extent. There had been little blood lost, and the patient had been given a transfusion of blood immediately afterward.

Autopsy.—The entire brain was removed and a tumor of the right frontal lobe was found; it weighed 230 Gm. In the neighborhood of the uncinate gyrus there appeared to be a small subcortical cyst projecting toward the interpeduncular space. The right hemisphere was definitely larger than the left; there was no pressure cone about the medulla. Dr. Grant, who removed the brain, was of the opinion that because of the large vascular channels and the extreme vascularity of the tumor, it probably would have been inoperable.

A Case of Chronic Encephalitis Presenting Cerebellar Symptoms. Dr. Alberta Jenkins.

History.—B. B., a white man, aged 18, began to complain of blurred vision, diplopia and severe, prolonged headaches one year before examination. Fever was not associated with the symptoms. Five months before, he began to have dizziness, staggering, nausea and vomiting, increased lacrimation and increased salivary secretion. Tinnitus and moderate photophobia were present. About this time he noticed that he would become drowsy and would frequently fall asleep while at school. The past medical history was irrelevant. He had never had epidemic influenza.

Examination.—The general physical examination gave negative results. The patient had no motor weakness or other pyramidal tract signs. There was no impairment of sensation. There was a fine tremor of the eyelids and of the tongue, and a tremor of the left hand which was somewhat suggestive of parkinsonism. In walking he did not swing his arms as much as the normal person. In the Romberg position he fell backward and to the left. In walking he staggered in the same direction with the eyes both open and closed, but much more with the eyes closed. When he attempted to rise from the floor without the aid of his arms, the feet were elevated, the left higher than the right. He did not flex the knees while bending backward, and would fall if not supported. The rebound phenomenon was present in the left arm. In bringing the arms downward from a vertical to a horizontal position, the eyes being closed, the left arm was held at a higher level than the right and the fingers were semiflexed and slightly separated. With the arms extended horizontally, pronation caused the left hand to be held higher than the right. There was slight hypotonia in the left upper extremity. The examination of the eye showed normal eyegrounds and no contraction of visual fields, but a distinct weakness of convergence. There was a diplopia in all fields. According to the audiometer tests hearing was within normal limits. The spinal fluid was under a pressure of from 4 to 6 mm. of mercury. Examination of the fluid showed two cells, a total protein of 1.7 (normal 1), normal globulin and sugar. The Wassermann test was negative. X-rays of the skull were normal.

According to the Bárány report, a lesion was localized in the left side of the pons.

Diagnosis.—The preponderance of cerebellar symptoms was striking. The absence of symptoms in the eyegrounds, the low spinal fluid pressure, the onset with diplopia, headache, vomiting, photophobia and periods of sleep resembling narcolepsy all made a diagnosis of chronic encephalitis most probable.

Comment.—Kawata described eight cases in which he found changes in the cerebellum as the result of epidemic encephalitis. The nucleus dentatus was particularly affected, and there were also changes in the Purkinje cells, and atrophy of the granular layer. In none of his cases does there seem to have been any distinct predominance of cerebellar symptoms. It would seem probable that in those cases of epidemic encephalitis in which cerebellar symptoms have predominated the pathologic changes would be more marked than in those described by Kawata.

DISCUSSION

DR. CADWALADER: Among the characteristic symptoms of cerebellar disturbances that Dr. Jenkins' patient presents is atonia, especially of the left upper limb. Most of us, I think, are inclined to overlook this sign of cerebellar disease because it is generally so inconspicuous in slowly developing lesions. In acute lesions, such as gunshot wounds of the cerebellum, atonia may be, in the beginning, the most conspicuous evidence of injury. By some authorities, the regulation of tone is regarded as one of the fundamental functions of the cerebellum, and the loss of tone, or atonia, the basis on which voluntary movements of the limbs in cerebellar disease become asynergic.

A CASE OF PARKINSON'S DISEASE EXHIBITING RHYTHMIC MOVEMENTS. DR. WILLIAM L. LONG.

G. C., aged 51, complained of nervousness, paresthesia of the back, change in personality and frontal headaches.

Positive physical symptoms included: pyorrhea, an old healed pulmonary lesion, a large soft prostate, a seborrheic skin, dermographia and myedema. When walking he did not swing the left arm. His other movements tended to be "en bloc."

Neurologic examination gave negative results except that the reflexes were all increased. There was a rhythmic flexion of the lower limbs occurring about twenty times a minute.

Positive laboratory observations were: basal metabolic rate, plus 8; phenolphthalein test, 30 per cent in two hours; spinal fluid under increased pressure, cell count 2, Wassermann test, negative; gastro-intestinal studies, x-ray of lungs and spine, eyegrounds and fields normal; serum calcium, 14 and carbon dioxide capacity of plasma 48 per cent by volume. A roentgenogram of the skull showed a calcified shadow in the posterior part of the middle fossa.

The case is presented as a case of Parkinson's disease with the unusual feature of the rhythmic flexion and extension of the lower limbs, and because of the fact that the headaches which were relieved by lumbar puncture were also relieved by moderate limitation of fluid intake.

Book Reviews

DIE HYSTERISCHE REAKTIONSWEISE. By DR. HANS KRISCH. Price, 4.50 marks. Pp. 97. Berlin: Urban & Schwarzenberg.

DIE WISSENSCHAFTLICHEN GRUNDLAGEN DER PSYCHOANALYSE FREUDS. By DR. M. NACHMANSOHN. Paper. Price, 7 marks. Pp. 106. Berlin: S. Karger, 1928.

Both these books belong to an increasing number which undertake a critical examination of the position of psychoanalysis in relation to normal and abnormal mental life, and both authors, as is customary, pride themselves on their freedom from all fetters binding them to the catechism of any particular school. Of the two, Krisch, who appears to have recently discovered psychoanalysis, is the more convinced of the great utility of Freud's theories and has allotted to himself the task of preparing in "usable form" the nuclei or principles of psychoanalysis for the classic psychiatrist. His avowed aim is to present not so much the negative as the positive aspects of psychoanalysis.

For after discounting all the exaggeration in the construction and generalizations of psychoanalysis, he believes that it has led to an important extension of psychologic depths, but on the other hand that it has already crossed its crest so that it will bring no essentially new contributions to psychiatry in the future. After chiding the psychoanalysts for their failure to accord greater recognition to the influence of constitutional factors, for the circumstantiality and vivid literary quality of their reports, for their demands of "belief without critical examination"—he begins to praise Freud enthusiastically for the application of the free association method, for the reexamination of sexuality which had lain inert since the work of Krafft-Ebing, for his research into the personality of infancy, etc.—all points by this time so universally acknowledged that their reiteration has become profitless. Krisch repeatedly interjects into the discussion his own conception of the hysterical reaction, which he believes, in the final analysis, depends on "the structure of the personality" and "that personalities in whom esthetic traits are connected with the components of the will" are especially prone to it — a vague, intangible, really empty definition.

It is in the chapter on treatment, however, that the author discloses his misconceptions and lack of grasp of psychoanalysis most flagrantly — not only in the practical application of psychoanalysis as a psychotherapeutic measure, but even in the definition of such commonly employed terms as "resistance" and "transference." One must conclude that, notwithstanding the author's laudable intention to act as a preceptor in psychoanalysis to the classic psychiatrist, the latter will do far better to seek his information at headquarters.

On the other hand, Nachmansohn, who is a doctor of philosophy as well as of medicine, is intimately acquainted with psychoanalytic literature and approaches his iconoclastic task step by step with methodical vehemence. As the theory of infantile sexuality is, as Freud himself emphasizes, one of the great fundamentals of psychoanalysis, Nachmansohn goes to great pains to prove its mythical character. He would bow before facts and gladly accept such a phase as a normal infantile sexuality, but claims that after twenty years of work psychoanalysis has up to the present time brought forth not a single fact in support of the existence of such a condition which would stand the test of scientific critique. Of the many psychologic theories which Freud has formulated, including those of the unconscious, dreams, symbols, slips of the tongue, wit, etc., Nachmansohn is willing to acknowledge the partial value of the concept of dream analysis in the understanding of mental life and admits the great significance which the theories of repression and regression have had for psychopathology. He believes, however,

that Freud overemphasizes sexual regression and that he fails to give sufficient consideration to the importance of philogenetic regression. As Nachmansohn rejects Freud's "assumption" of an infantile sexuality as not proved, he must necessarily deny the validity of speaking of regression to such a nonexistent stage.

In his lengthy attack on the dream theory, Nachmansohn displays considerable dexterity in exposing some of the more vulnerable elements, especially the utilization of free associations as indicative and interpretive of the latent dream content, in demonstrating the difficulties of establishing the wish fulfilment character even in some dreams of children and Freud's ingenious though not entirely convincing postulate of a reception compulsion in the dreams of traumatic neurotic persons. His own favorable admissions here and there, however, and the psychoanalytic concepts which he has unconsciously embodied in his discussion tend to negate his sweeping statement at one point that "that which is new in Freud's theory is not tenable, that which is tenable is not new."

The briefest and at the same time the most inaccurate portion of Nachmansohn's critique is that of the psychoanalytic technical approach. For instance, he believes that "the abandonment of catharsis seems to me to have been fatal to the development of psychoanalysis. Through this it became possible for the analyst to avoid the affirmation of his interpretations by the patient" (p. 100). Of course, catharsis still remains an integral part of psychoanalysis. Moreover, Freud does ignore the quantitative factor of reactions and considers them only qualitatively; he does not even maintain that the associations to a dream always have bearing on the manifest content of the dream, that the difficulties of overcoming resistance are not universal, and that the analyst may not at times seek the cause of resistance without success.

The more one becomes acquainted with the criticisms of psychoanalysis from extra-psychoanalytic sources, the more evident does it become that the future progress and advances in psychoanalysis must come from within. The ruthless overhauling to which Freud, even at his advanced age, is constantly subjecting his earlier theories, as shown in "Hemmung, Symptom und Angst" published in 1926; the keenly critical attitude toward moot points within the psychoanalytic ranks; the unceasing effort to improve and shorten technic; the researches which aim to reconcile the psychoanalytic interpretation with physiologic developments and recent investigations into the structure of the ego are all indications that psychoanalysis has not "crossed the crest" but may in the future render even more valuable service to psychiatry in particular and to medicine in general.

NEUROLOGICAL EXAMINATION. By CHARLES A. MCKENDREE, M.D. Price, $3.25. Cloth. Pp. 289, with 88 illustrations. Philadelphia: W. B. Saunders Company, 1928.

During recent years a number of books have been published on the methods of examination of the nervous system. This seems to be by far the best, however, because it has an anatomic and pathologic point of view.

It is by no means easy to make a comprehensive examination of the nervous system, particularly an examination of sensibility. Most students, undergraduate and graduate, have difficulty in finding books which give sufficiently illustrated methods of obtaining symptoms. What is more difficult is to have these symptoms, once obtained, properly interpreted in terms of pathology. This author, however, does that and does it well. The one criticism that can be offered is that there are not enough illustrations. While the description of the methods of examination for the neurologic status is satisfactory though wofully inadequate, that for the mental status comprises only eleven pages which might better have been omitted.

PRESCRIBING OCCUPATIONAL THERAPY. By WILLIAM RUSH DUNTON, JR. Price, $2.10 and $1.35. Pp. 142. Springfield, Ill.: Charles C. Thomas, 1928.

Occupational therapy is occupying the attention of physicians more and more. This is particularly true of those in hospitals. The value of occupational therapy has long been known and utilized in hospitals for patients with nervous and

mental diseases, but its value in general medical, surgical, orthopedic, cardiac and tuberculous disorders has not been given the appreciation that it deserves. This book, by William Rush Dunton, who is a pioneer in the subject, is timely. The value of different types of occupational therapy in the various special fields of medicine is described. The book is particularly valuable to physicians in institutions and general hospitals.

LECTURES IN PSYCHIATRY. By WILLIAM A. WHITE, M.D. Price, $3. Pp. 166. Washington: Nervous and Mental Disease Publishing Company, 1928.

In a series of twelve lectures on psychiatry Dr. White describes most of the major psychoses. It is always somewhat of a feat to describe any of the psychoses in such a manner that the reader will carry away a comprehensive impression of the salient points. Dr. White, however, has done this. In a book of 158 pages he gives the reader an excellent point of view of the commoner and major psychiatric disorders.

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